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CERTAIN ASPECTS OF THE CHEMISTRY OF INFECTIOUS DISEASES¹

By Dr. M. L. CROSSLEY

DIRECTOR OF RESEARCH, CALCO CHEMICAL DIVISION, AMERICAN CYANAMID COMPANY

THE discovery of microorganisms as the causative agents in infectious diseases introduced a new problem of relating the specific characteristics of a disease to the nature and behavior of the particular type of organism responsible for the pathological condition. It seemed reasonable to expect that the infecting agent would change the normal course of certain physical and chemical processes essential to the regular functions of the healthy state of the animal. A knowledge of the mechanism of the cycle of events involved would lead to a rational basis of treating the disease to eliminate the difficulties and reestablish normal conditions. Obviously, it was of prime impor-

tance to learn as much as possible about microorganisms and their pathogenicity before a comprehensive study of their rôle in disease would be instructive and profitable. Just how the infecting agent causes a specific disease, what changes occur, where these changes are initiated, the nature of the resulting products and their influence on the physical and chemical process underlying the normal cellular activity of the animal; are questions which must be answered before chemotherapy can be highly effective in relieving man of the many ills that now reduce his efficiency, limit his usefulness and endanger his life.

All these questions involve difficult problems. The infecting agents are themselves complex organisms, whose metabolic processes are poorly understood. The animal organism is much more complex and its

¹ Address delivered before the general meeting of the American Chemical Society at the Detroit meeting September 9, 1940.

cellular activities so numerous and varied as to render difficult if not impossible direct experiments at the seat of the trouble. The indirect approach thus necessitated in research of this kind leads to uncertainties in the interpretations of the results. Even if micro-organisms worked like termites, boring into animal tissues and thus reducing their strength, impairing their efficiency and jeopardizing their life, it would still be a difficult task to examine the nature of the damage done and relate it to the cause of the trouble. A man can not be sawed into pieces like a log for inspection nor can he be subjected to physical and chemical tests in the ordinary laboratory equipment.

In spite of the fact that much has been learned about the chemistry of animal metabolism since the discovery of the microbe nature of the causative agents in infectious diseases, little or nothing is known about the chemistry of these diseases. What evidence there is seems to indicate that the blood may be expected to show marked changes in composition, reflecting the effect of the infection on tissue metabolism. Certain changes may occur in the serum proteins and possibly in the enzymatic processes of this and other tissues in the animal body.

Changes in the solid content of the blood with variations in the albumin-globulin ratio of the serum proteins have been observed in certain infectious diseases. In such cases the globulin increases in proportion to the severity of the disease. In acute fevers the viscosity of the blood is reported to increase.² Changes occur in other tissues. During the fever stage in pneumonia³ there is a decrease in vitamin A of the liver with a correspondingly high output in the urine. The glucosamine in the blood serum is significantly higher in pneumonia.⁴ The plasma lipids are said to drop to abnormal levels⁵ and may be controlled by the early administration of serum. In tubercular meningitis the sodium chloride content of the cerebrospinal fluid drops to the unusually low level of about 510 mg per cent.⁶ The normal value is about 700 mg per cent. Also, in tuberculosis there is a decrease in the coloring matter of the blood without a corresponding decrease in the iron.⁷ The serum proteins are said to decrease during the progress of tuberculosis.⁸

The available evidence is not convincing enough to permit much stress on the significance of the chemical changes and the specificity of their nature in relation

to definite causative agents of disease. A major difficulty in evaluating the results is the uncertainty that all the important factors influencing these results were known and appreciated. The infecting agent which under certain conditions would produce infection in experimental animals may at other times have little or no effect due to protective agencies which in some unknown way offset the effect. The susceptibility of the animal varies widely. The factors governing this are unknown. There is no way at present of measuring the capacity of an animal to resist infection. It is undoubtedly a complex cycle of cellular events in which highly reactive chemical substances play important rôles. Vitamins and enzymes are the chemical compensators which help to establish and maintain the immediate degree of livingness of the organism. If there was some way of measuring this it might be designated as "the living potential" of the organism.

From the available evidence it seemed likely that a significant change might be expected in the relation between sulfide and sulfhydryl sulfur of the tissue proteins in infectious diseases. Brdicka, using the Heyrovsky polarograph,⁹ had shown significant differences between the polarographic waves obtained on electrolyzing blood sera of normal persons and of those having cancer.

The polarograph is essentially an electrolytic apparatus in which mercury serves as the electrode. The cathode is formed by mercury dropping at a definite rate from a glass capillary of about .05 mm diameter. The collecting layer of mercury serves as the anode. A direct current is passed through the electrolytic solution under increasing voltage and the current-voltage curve recorded photographically. The curves so obtained are reproducible with a fair degree of accuracy. Only a few cc of solution are required for the electrolysis. When protein is present in the dilute electrolytic solution of ammonium chloride a characteristic wave is produced on the current-voltage curve and this effect is believed to be due to the electrolytic evolution of hydrogen catalyzed by the presence of the protein at the cathode interphase. Brdicka,⁹ studying this protein effect, found that in buffered cobalt-ammonium chloride solutions a characteristic "double wave" was produced on the current-voltage curve by proteins containing sulfur. He ascribed this double wave to available sulfhydryl and disulfidic groups in the protein and showed that the height of the protein wave was a significant indication of changes occurring in the proteins during pathological conditions and could be used as a valuable aid in diagnosing cancer. It was also shown that cystine and other thio acids produced a similar catalytic effect with divalent cobalt in the buffer solution. The polypeptides and proteins

² Bachmann, *Deutsch. Arch. f. klin. Med.*, 94: 409, 1908.

³ T. Lindquist, *Klin. Wochschr.*, 16: 1345, 1937.

⁴ Ivar Nilsson, University of Upsala, *Biochem. Zeit.*, 291: 254-8, 1937.

⁵ A. V. Stoesser, *Proc. Soc. Exp. Biol. and Med.*, 43: 168, 1940.

⁶ John Ingram, *Brit. Med. Jour.*, July, 1937, p. 111.

⁷ Wells and Long, "Chemistry of Tuberculosis," p. 225.

⁸ *Ibid.*, p. 231.

⁹ Heyrovsky, *Nature*, 142: 317, 1938.

gave the effect with both divalent and trivalent cobalt. Other investigators have confirmed the essential facts and the polarographic method has been shown to be a valuable means of studying certain biochemical reactions.

The height of the characteristic protein double wave is lower for cancer sera than for normal. Likewise, it has been shown that a more pronounced difference can be obtained by comparing the sera after controlled denaturation and precipitation of the macroproteins with sulfosalicylic acid. The height of the wave of the unprecipitated fractions, so obtained, designated "peptone fraction," of a cancer serum is greater than that of the normal serum when measured under the same conditions in the same trivalent cobalt-ammonium salt buffer. Brdicka¹⁰ interpreted these results to mean that the two types of sera had different amounts of available sulfhydryl sulfur and that this polarographic result was in harmony with the results previously obtained by A. Purr and M. Russel, who found that carcinomatous blood was less active in certain biological reactions than normal blood. E. Waldschmidt-Leitz and his collaborators ascribed this lower activity of carcinomatous blood to the presence of fewer sulfhydryl groups in the carcinomatous serum.

A limited number of results with various inflammatory conditions indicated that this polarographic method might prove to be useful in the study of the blood sera in the infectious diseases that interested us. By this means it was thought possible to get some idea of the chemical changes occurring in the tissue protein in different infectious diseases. We elected to study first experimental pneumococcus pneumonia in dogs, using the technique of Terrell, Robertson, and Coggeshall¹¹ for infecting them. By this technique, that is the direct introduction of the infecting agent into the lungs, it is possible to produce in dogs a pneumococcal pneumonia which resembles closely the corresponding disease in man. In this way the disease can be studied under controlled conditions. Such a study should furnish information of value as to the nature of the disease, the chemical changes involved and the chemotherapy most likely to be successful in combating it. Until these fundamental data are established the treatment of infectious diseases in man will remain highly empirical and unsatisfactory.

A careful study of the blood sera of several normal dogs was made to establish a basis for comparison and also to demonstrate the reproducibility of the polarographic method in this case. The results were highly satisfactory and justified the further applica-

tion of the method to the study of the blood sera of the pneumonia dogs.

The height of the characteristic wave of the polarogram for the whole serum in this type of pneumonia¹² is lower than normal. This is consistent with Brdicka's findings for carcinomatous serum and would seem to indicate that in both pathological conditions there is a decrease in polarographically active protein groups and in experimental pneumonia it would appear also that there is an actual decrease in serum protein since the protein nitrogen is lower than normal.

A more significant result is the change manifested in the peptone fraction of the pneumonia serum. There is a marked and progressive rise in the height of this characteristic wave accompanied by a change in the shape of the wave with the increase in the severity of the disease, reaching a maximum at the height of the pneumonia. With recovery the wave height drops continuously until it reaches the normal value and the curve assumes the normal shape. The nitrogen values rise with the corresponding increase in the height of this significant wave confirming the fact that there is a progressive change in proteins of the blood serum with the advance of the disease and this leads to increase in protein degradation products in the denatured protein.

The changes in the current-voltage curves of the blood serum of the pneumonia dogs are not confined to the fever stage of the disease. This is over, as a rule, before the maximum effects are obtained. The fever is but one symptom of the disease. It may or may not be indicative of significant physical and chemical changes in the tissues, particularly those tissues directly involved; in pneumonia, lung tissue. That definite changes occur in the metabolism of the lung tissue in lobar pneumonia is to be expected from the nature of the disease. It has been shown previously¹³ that the environmental conditions of the cells change and with the rapid growth of pneumococci, the engorgement of the capillaries, and the filling up of the air cells with serous material the oxygen supply from the inspired air is diminished to a degree which makes the normal cellular metabolism difficult if not impossible. The oxidation processes in the congested area must then depend upon a supply of oxygen from the venous blood. Under these conditions the glucose content of the tissues diminishes and lactic acid increases. There must be also certain products of the bacterial metabolism which may influence the physical and chemical processes of many cellular structures throughout the animal body. Since the cellular processes appear to be regulated by a finely adjusted

¹² Crossley, Kienle, Vassel, Christopher. In press.

¹³ Friedemann and Graeses, *Jour. Exp. Med.*, 67: 481, 1938.

¹⁰ Brdicka, *Col. Czech. Chem. Comm.*, 5: 112, 148, 238, 1933.

¹¹ Terrell, Robertson, Coggeshall, *Jour. Clin. Investigation*, 12: 393, 1933.

mechanism in which liver cells play an important rôle, the effects of the bacterial invasion may be far-reaching and necessitate adjustments which tax the reserve power of the organism beyond the limit of its capacity.

The question is: are the effects shown by the polarograph the result of the infection or the manifestation of the chemical changes involved in the readjustment of the system to meet the new conditions imposed by the bacterial invasion. Obviously this question can not be answered fully with the available evidence. We do not yet know the full significance of the changes in protein as indicated by the current-voltage curves. From the resemblance of these with the curves obtained with cancer sera and also with the sera from a limited number of patients suffering from different inflammatory conditions it would seem that the effects we get are not entirely specific for pneumonia. Of course, further study may reveal some phase of the effect which is definitely related to the peculiar conditions of pneumonia and lead to a better understanding of the disease. We can not tell from the evidence if the changes in the proteins are of the same type and follow the same course. It is possible that the cleavage of the proteins follows a definite pattern laid down by the enzymatic tools furnished by the specific bacteria. From our results it appears that not only do the sera from the pneumonia dogs give progressively higher peptone values when denatured but also show increasing amounts of such degradation products in the whole sera with the progress of the disease.

Preliminary results indicate that the treatment of the experimental pneumonia with sulfanilamide and sulfapyridine did not affect either the height or the shape of the characteristic current-voltage curves. This was also true of normal dogs given these drugs. Their curves were similar to those previously obtained when no drug had been administered. Whatever the function of these drugs in curing the disease, there is no evidence that they influence the course of the disease as indicated by the protein changes manifested by the polarographic results. This may mean that the essential function of the drug is to aid in destroying the bacterial infection and thus bring about a check of the disease. The blood changes measured by the polarograph may be part of the result of the infection and may run a regular course which is not effected

by the chemotherapy. Further information should throw more light on this phase of the problem.

Besides, the cystine values of the whole sera of the pneumonia dogs are lower than those for the normal animals. The cystine drops progressively with the advance of the pneumonia until it reaches a minimum at the height of the disease. Then, if the animal recovers, it begins to rise and continues upward until it reaches the normal level, when the dog is well. This runs parallel with the rise and fall in the typical peptone wave. It also seems from the preliminary data that with rapid onset and severity of the pneumonia there is a correspondingly rapid decline in the cystine values. The drop in cystine corresponds to the decrease in total nitrogen of the serum and is additional evidence that the sera of the pneumonia dogs contain less proteins than those of the normal animals.

These polarographic results are consistent with the evidence obtained from the x-ray photographs showing the progress of the pneumonia. With the increase in the congestion of the lungs there is a rise in the peptone wave or increase in protein degradation products. Correspondingly there is observed a fall in the cystine, this tending to reach its minimum value when the pictures show the congestion at its height. Similarly, when the x-ray pictures show the dog to be improving, that is a progressive resolution of the involved areas, the polarograms also show the animal to be returning to normal. In general the polarographic results seem to give a more accurate picture of the animal's condition, showing a steady progress toward normalcy when the x-ray pictures fail to show definite evidence of the disease. The animal appears well before the polarograms indicate this condition.

While these results are interesting and appear to be significant they are not complete enough to justify a conclusion as to the specific chemical changes in pneumonia and relate cause and effect in connection with the manifestation of the symptoms of the disease. The investigation continues and it is hoped that in time sufficient data will be secured to allow of a definite correlation of the chemical changes and the symptoms of the disease. Such results would help to provide a rational basis for chemotherapy and improve the efficiency in predicting what chemical agents will have the greatest chance of success in combating infectious diseases.

THE IMPORTANCE OF MICROORGANISMS IN VITAMIN RESEARCH

By Professor ROGER J. WILLIAMS

THE UNIVERSITY OF TEXAS

THE beneficial relationships of bacteria and microorganisms to mankind are almost as well recognized as their harmful effects. In very recent years, how-

ever, these tiny distant cousins have become useful to man in an entirely new way.

The history of their usefulness in vitamin research

goes back to 1901—ten years before the term “vitamin” was coined—when in Ide’s laboratory in Louvain, Belgium, it was discovered that yeast plants require for their proper nutrition something which was then called “bios” but is now known to be essentially a mixture of several of the water soluble “B vitamins.”

A relationship of “bios” to what we call vitamins was first definitely established when it was found in the author’s laboratory about ten years ago (1930) that pure vitamin B₁ had, under appropriate conditions, a tremendously stimulating effect on yeast growth and hence was a constituent of the hypothetical “bios” discovered about thirty years before.

A second link between “bios” and vitamins has become apparent since pantothenic acid has been demonstrated to be a vitamin required by all animals which have been tested. This substance was discovered and isolated in the writer’s laboratory, because of its stimulating effect on yeast growth and was undoubtedly a highly important constituent of the original “bios.” It appears to be a universal constituent of all types of living matter and to be part of a metabolic mechanism common to all living things.

Three more links between “bios” and vitamins have been discovered within the past two years—two of them within a few months. Pure vitamin B₆, now called pyridoxin, was found to be effective as a stimulator of yeast growth, and hence it may be deduced that it was also a contributing factor toward the original “bios” effect.

One of the most recent findings relating “bios” to vitamins has to do with the very interesting substance “biotin” discovered and isolated by Kögl in Utrecht. This substance stimulates yeast growth under conditions quite different from those used in Ide’s laboratory in 1901, but was nevertheless one of the several effective substances present in the original “bios” mixture. It, too, is a vitamin as has been demonstrated very recently by György and du Vigneaud, and the name “vitamin H” will now drop out of the literature and be replaced by the name *biotin*, which is that of a single definite substance.

The latest connecting link between the old “bios” and vitamins came with the discovery by Woolley that inositol is a vitamin required by at least one animal—the white mouse. Inositol as a chemical substance has been known for decades. It was discovered in the late Lash Miller’s laboratory in Toronto to be a “bios” constituent over a decade ago, but it has been only within a few months that it has been found to be a necessary constituent of the food of an animal.

It is a highly significant fact that every one of the five pure substances known possess “bios” properties, namely, thiamin (vitamin B₁), pantothenic acid, pyridoxin (vitamin B₆), biotin (vitamin H), and inositol is, without exception, a vitamin required by animals.

Conversely, most of the known members of what was earlier called the “vitamin B complex” have under proper conditions at least some “bios” activity. If vitamin chemists had years ago set out seriously to determine what “bios” is, they would have discovered most of the members of the “vitamin B complex” which are now known. Because testing with yeast, though not without pitfalls, is incomparably more rapid than testing with animals, it is reasonable to assume that progress would have been much more rapid using the “yeast route” than it has been using animals as test organisms.

But yeasts are not the only microorganisms which have yielded results which are valuable from the standpoint of vitamins and if the hypothetical vitamin chemists mentioned above had broadened the scope of their investigations and had investigated the nutrition not only of yeasts but of other non-pathogenic microorganisms (and excluded animals from consideration), they would have found *all* the members of the “vitamin B complex” which are now known. The vitamin-like properties of nicotinic acid (which as a chemical compound had been known for many years) were in fact first discovered by Knight in England, who found it to be essential for the growth of *Staphylococcus aureus*. This finding was rapidly followed by the discovery of Elvehjem and coworkers that nicotinic acid (or its amide) is the anti-pellagra vitamin and will cure black-tongue in dogs.

Riboflavin (for a time called vitamin B₂) is one of the “B vitamins” which under ordinary conditions has not been observed to affect yeast growth in any striking way. It, like pantothenic acid and several other “B vitamins,” is required by lactic acid bacteria (among others) and it could have more readily been discovered using these organisms than by using animals.

It is hardly profitable, of course, to discuss at length what might have happened if vitamin research had taken a different course. It is interesting, however, to note that microorganisms have played a leading role in the discovery of four of the seven members of the “vitamin B complex” which have been isolated or identified as possessing vitamin properties, *i.e.*, pantothenic acid, nicotinic acid, biotin and inositol.¹ This is in spite of the relative lack of emphasis on microbiological nutrition.

It is not only in the discovery of vitamins that microorganisms have been and will be useful. They may be expected to play an important part in the discovery of how vitamins function in the various enzyme systems.

A most important requirement necessary for the

¹ Since the above was written, another member of the “B family” of vitamins, *p* aminobenzoic acid, has been identified by Ansbacher. It represents an additional case in which studies with microorganisms have led to the identification of a vitamin.

study of how and where vitamins function is that methods be available for their quantitative determination. Though each individual substance presents its peculiar problems it is safe to say that microbiological methods are destined to play a highly important role in the future determination of "B vitamins." The microbiological methods can be rapid and fairly accurate, and at the same time they can be applied to extremely small amounts of material.

Workers now associated with the writer have described acceptable assay methods for three of the "B vitamins," namely, riboflavin, pantothenic acid and biotin. Methods for others will be forthcoming shortly from our laboratory at the University of Texas. E. E. Snell, in the writer's laboratory, has been a pioneer in this field. The usefulness of these methods is particularly outstanding when the available material to be tested is far too little to be used in animal tests and even too small for most chemical tests, in case such are available.

Investigations with microorganisms have made it seem apparent that the "B vitamins" (or at least some of them) are more fundamental and of more far-reaching importance than the other vitamins. This is true in the sense that they function in the mechanisms of diverse forms of life. I believe there is no reason to think that vitamins A, D, E, K, or even C, function

in the life of yeast cells, and for other microorganisms also they may be unimportant. The recent observation that cockroaches can be raised to maturity without vitamin A and that an assay of their bodies indicates its absence, is further evidence regarding non-universality at least of this one fat-soluble vitamin. On the other hand, so far as thiamin, pantothenic acid, nicotinic acid, biotin and riboflavin are concerned, the evidence indicates that they may be present and function in all forms of life from the highest to the lowest. These five have not been investigated with equal thoroughness. The two other "B vitamins," pyridoxin and inositol, have been investigated even less thoroughly but appear to be very widespread.

Summary: In spite of a general lack of emphasis on this field, yeasts and other microorganisms have been used in the discovery (and/or isolation) of four out of seven of the recognized members of the "vitamin B complex."¹ Their use in the study of how vitamins function shows much promise, particularly in that methods have been worked out or are in process of development for determining quantitatively on a micro-scale practically all the members of the B family of vitamins. Indications are cited that the "B vitamins" are unusually important, i.e., for all forms of life, in contrast to the other vitamins which appear not to be universally distributed.

OBITUARY

HERBERT FREUNDLICH 1880-1941

HERBERT FREUNDLICH was born in Charlottenburg, Germany, on January 28, 1880, and died suddenly in Minneapolis, Minnesota, on March 30, 1941, of a coronary thrombosis.

Professor Freundlich was the son of Phillip and Ellen (Finlayson) Freundlich. He graduated from the gymnasium in Wiesbaden in 1898. He studied general science for one year at the University of Munich and then specialized in chemistry at the University of Leipzig under the distinguished leadership of Professor Wilhelm Ostwald. Here in 1903 he took his Ph.D. degree with a dissertation dealing with the coagulation of colloidal sols by electrolytes.

For the following eight years Professor Freundlich remained at the University of Leipzig, teaching analytical and physical chemistry, attaining the rank of Privatdocent in October, 1906, on the basis of his studies on adsorption from solution.

He was called to the professorship of physical chemistry and inorganic technology at the Technische Hochschule, Braunschweig, in the autumn of 1911. Here he remained until February, 1916, when at the invitation of Fritz Haber he joined the staff of the Kaiser

Wilhelm Institut für Physikalische und Electrochemie at Berlin-Dahlem to conduct and direct research work on the adsorption of war gases and to study charcoals and other adsorbents for use in gas mask canisters. In these studies he achieved notable success.

In January, 1919, he resigned his professorship at Braunschweig to remain permanently at the Kaiser Wilhelm Institut as chief of the Division of Colloid Chemistry and Applied Physical Chemistry. Still later he was appointed associate director of the Institut.

In 1923 he was made honorary professor of chemistry at the University of Berlin, and he received the same honor in 1930 from the Technische Hochschule of Berlin. In 1925 he accepted the invitation of the University of Minnesota and the Colloid Committee of the National Research Council to be guest scholar at the second National Colloid Symposium held at the University of Minnesota, and he remained in residence at Minnesota, giving a series of lectures on colloid chemistry in the following summer session. Here he captivated his American colleagues by his charming personality and established many enduring friendships. The invitation to be foreign guest scholar at the fourteenth annual National Colloid Symposium at the Uni-

versity of Minnesota was repeated in 1937, and again he remained at the university for a series of lectures in the following summer session.

Following the rise of the Nazi régime, Professor Freundlich was ordered in the spring of 1933 to dismiss all his associates who were not of the "pure Aryan" race. As a result of this order he resigned in protest and soon left his native land for the greater intellectual and scientific freedom which England afforded. Here in England he became associated with University College, London, through funds provided by Imperial Chemical Industries, Ltd., on the initiative of Professor F. G. Donnan and other eminent British scholars. In this post he remained until January, 1938, when he was called to the University of Minnesota as distinguished service professor of colloid chemistry in the graduate school of the university without college or departmental assignment. In this new and unique position Professor Freundlich could and did accept major responsibilities for graduate students from a variety of fields such as physiological chemistry, biochemistry and physical chemistry, and was frequently consulted by other students working in physics, physiology, etc. In the short time that he held this post at Minnesota, besides carrying on teaching and research in his own specialized field, he came also to fill the post of an "elder statesman" who was frequently consulted by both colleagues and students and from whom sound and disinterested advice was always available.

Professor Freundlich's scientific career lay almost wholly in the field of colloid and capillary chemistry. This field, since Thomas Graham (1805-1869), had lain largely dormant in the years which saw the rise of both synthetic organic and physical chemistry. In 1903, when Freundlich published his doctorate thesis, only 23 titles dealing with colloids or colloidal behavior appeared in all the world's chemical literature. This year (1903) the names of Freundlich, Jean Perrin, W. O. Pauli, G. Bredig and W. B. Hardy bespoke the inauguration of a new era, and not the least of these masters was Herbert Freundlich.

Freundlich's interest in colloids and colloidal behavior developed from his fundamental interest in biological phenomena and he, like Sir W. B. Hardy, turned to colloid chemistry in the hope of finding tools with which to attack a study of the mechanisms underlying protoplasmic behavior.

His classical studies on the coagulation of colloidal sols by inorganic and organic electrolytes was shortly followed by his studies on adsorption from solution and his demonstration that this represented a true reversible equilibrium which was obeyed by systems of the most diverse sorts. These studies culminated in

his discovery that adsorption was another manifestation of the Gibbs theorem relating the interfacial concentration with interfacial energy relationships.

In the more than 200 papers and in the several books which he published we find important original concepts relating to almost every field of colloid research or technology. His studies of the electrical behavior of colloids and his fundamental concept of the zeta-potential are classical, as are his studies on the optical properties of sols, especially systems containing anisotropic and anisometric particles, which field bids fair to become a new area of optical science. His studies on the mechanical properties of sols and gels, swelling pressure, thixotropy, rheopexy, dilatancy and ultrasonic behavior in colloid systems have all introduced new and fundamental concepts and techniques.

While many of his contributions to colloid science have already received their merited recognition, we are still probably too close to others to properly appreciate their importance. This, however, can not be said for his "Kapillarchemie," which has gone through four German editions (1909-1932), numerous reprintings, and English (1926) and Russian translations. This book alone would have justified the high scientific eminence which Freundlich attained.

Professor Freundlich received many honors for his scientific contributions. Besides being elected to numerous scientific societies and academies he was honored by the University of Utrecht in 1936 with the degree of doctor of philosophy *honoris causa*, and in 1940 while at the University of Minnesota he was elected a foreign fellow of the Royal Society.

In 1908 he married Marie Mann, daughter of an apothecary in Mainz. Two sons and two daughters were born from this union. Three children survive, Herbert Freundlich, Jr., a radio research physicist now residing at Cambridge, England, a daughter, Marie, in Holland, and a daughter, Kate, of Rochester, Minnesota. His wife Marie died in 1917 and Professor Freundlich in 1923 married Hella Gellert, who survives him.

This appreciation would be incomplete without a word regarding Freundlich the man. Professor Freundlich was modest, unassuming, always ready to assist any one who came to him for advice or counsel on either scientific or private affairs. His advice was always freely given, the thought of receiving credit for ideas never crossing his mind. Such personal traits endeared him alike to his colleagues and his students; the latter often referred to him as "Uncle Herbert." He was an accomplished pianist and greatly enjoyed the world of music. His early scientific interests in entomology were continued through life. His literary interests were wide and profound.

To-day many of those who have worked with him hold leading positions in the realm of colloid science. We who have prepared this note are confident that these former students and colleagues would wish to

join with us in mourning the passing of one of science's noblemen.

ROSS AIKEN GORTNER
KARL SOLLNER

THE UNIVERSITY OF MINNESOTA

SCIENTIFIC EVENTS

THE INSTITUTE OF GEO-BIOLOGY IN PEKING

DURING the summer of 1940, the laboratories, the library and the most important specimens of the Huangho-Paiho Museum, founded in 1915 and directed for twenty years by F. Licent, have been transferred to Peking, where the work will be continued under the name of "The Institute of Geo-Biology."

Officers of the institute at Peking are P. Teilhard de Chardin, geologist-paleontologist, honorary president, and P. Leroy, zoologist, director. Members of the staff are M. Trassaert, geologist, and J. Roi, botanist.

An official statement has been issued which reads:

In itself this change of location, decided for external circumstances, is purely material. But, more deeply, it means an internal transformation resulting from the natural growth of the institution.

The original idea of F. Licent, when he began pioneering in China, was to collect and study in Tientsin all possible data concerning the natural history of the Huangho basin. Following this trend of activity, we had come to the conviction that China was the place for an Institute devoted to the systematic development of what might be called the Science of "continental evolution." From both geological and biological points of view, Continents represent a kind of natural unit. Either in their building under tectonical and eruptive forces,—in the nature of their sediments,—in the formation and the shifting of their basins,—in the modelling of their topographical surfaces,—in the variations of their climates,—or in the development and the distribution of special vegetal and animal groups, they can only be studied "as a whole." And, if understood as a whole, they may introduce us to a renewed and better conception of the mysterious "concrecence" of Land and Life which is the Earth around us.

Hence the idea of an Institute of Geo-Biology where an associated Group of Geologists, Zoologists and Botanists would try, using the exceptionally distinct continental features of Asia, to draw, along as many directions as possible, a series of "blockdiagramms" expressing the joint evolution of rocks and organisms over China in the course of time. In a next-Memoir, for instance,¹ one of us (P. Leroy) will experiment with this method for the thick-shelled Unionids of Eastern Asia. Similar studies will follow, we hope, tracing, in the case of Mammals, the development of Asiatic Mole-rats (*Myospalacinae*), *Duplicidentata*, etc.

Being, as told above, the direct continuation of the Huangho-Paiho Museum, the Institute of Geo-Biology is not, strictly speaking, a new creation. Still less does it

involve any shadow of competition with such sister-institutions as the Geological Survey of China, the Cenozoic Laboratory of Peking, the Fan Memorial Institute, the Heude Museum of Shanghai, the Natural History Society of China, etc. In fact, for the time being, the Institute will not print any publication of its own, but merely will distribute, as separates, its various contributions to the already existing scientific periodicals in China.

To cooperate, just as we did before, with the general effort of our friends, but with a more definite and more efficient line of investigation, such is the aim of the Peking's Institute of Geo-Biology.

The institute will be grateful for any exchange of publications, and "it is heartily ready to communicate any data, which might lead to a better understanding of the life of a continent."

THE ELLEN H. RICHARDS INSTITUTE

THE trustees of the Pennsylvania State College have established the Ellen H. Richards Institute as a consolidated working research unit covering some of the investigations formerly carried on in the departments of chemistry and of home economics and in the Agricultural Experiment Station.

Studies in textile technology, which have been carried on at the college in the department of chemistry since 1919, will be included in the work of the new institute. These have been concentrated on investigations on the durability of textile articles in relationship to fabric construction and types of dyes, and on methods of laundering and dry cleaning. Research fellowships are maintained at the college by the Pennsylvania Association of Dyers and Cleaners, the Pennsylvania Laundryowners Association and the Pennsylvania Institutions of Welfare, Public Instruction, Health and Military Affairs.

Research studies in human nutrition, begun at the Pennsylvania State College in 1935, will also be continued in the Ellen H. Richards Institute. These include an investigation on the relationship of dietary intake to family nutritional status, and a similar study in child nutrition begun cooperatively with the Department of Health of the Commonwealth in 1936. Efforts to change nutritional status for the better by such means as parental or child education and the provision of a school lunch have been tried and the results measured.

Investigations of the suitability of many new materials for the construction of houses or parts of houses,

¹ To be published in *Palaeont. Sinica*.

and of the performance of various new types of household equipment have recently interested some of those working at the Pennsylvania State College, and a study of some of these physical aspects of housing is an immediate prospect.

The institute was named for the first woman to receive a degree in chemistry from one of the great institutions of learning and research in the country, the Massachusetts Institute of Technology. As a research chemist and teacher, Ellen H. Richards (1842-1911) devoted her professional life to the application of chemistry and of the scientific method to improving home living conditions, and to establishing household science as a field of study in the improvement of standards of living.

Dr. Pauline Beery Mack, director of research in home economics, who has been on the staff of the School of Chemistry and Physics at the Pennsylvania State College since 1919, will be the first director of the institute, which will be administered jointly through the School of Agriculture and the School of Chemistry and Physics.

EXCHANGE OF ASTRONOMICAL PAPERS WITH FOREIGN COUNTRIES

ASSOCIATE PROFESSOR BART J. BOK, of Harvard Observatory, is chairman of a committee of the American Astronomical Society through which the exchange of astronomical papers is now proceeding regularly in the United States, England, Germany, France, Italy, the Netherlands, Belgium and Poland. Other members of the committee are James Stokley, of Science Service, and Dr. Herbert R. Morgan, principal astronomer, U. S. Naval Observatory. Arrangements for the exchange were begun last September, and have been in effect since December. The Royal Astronomical Society accepted this month the invitation of the American committee to join in the exchange. Under the arrangement astronomers in England and continental Europe are sending scientific papers to Harvard University for mutual exchange.

At least once a month the American Committee, which has mailing headquarters at the Harvard Observatory, ships copies of *The Astrophysical Journal*, *Publications of the Astronomical Society of the Pacific*, *Popular Astronomy* and *The Telescope*, together with abstracts and papers from various observatories, to astronomers in Leyden, Berlin, Brussels, Paris, Florence and London. These astronomers attend to the circulation of the literature to investigators in their own countries. Many American observatories are participating in the plan by sending copies of their publications.

Dr. Bok stated that judging from the scientific papers received at the Harvard Observatory from England and Germany research in astronomy in these

countries is at about one half its normal activity; in the occupied countries astronomers have resumed almost normal activity.

ARMY SERVICE OF MEDICAL STUDENTS AND INTERNS

A RESOLUTION has been adopted by the Committee on Public Health Relations of the New York Academy of Medicine urging that the drafting for Army service of qualified candidates for admission to medical schools, medical students and medical graduates serving as interns in approved hospitals, be deferred until their medical training is completed. The resolution was transmitted in a letter addressed by Dr. Malcolm Goodridge, president of the New York Academy of Medicine, to the President of the United States. The letter reads:

I hope that your appeal for a thousand volunteer physicians for Great Britain may meet with adequate and immediate response. When the press asked my opinion concerning your appeal, I did not hesitate to endorse it wholeheartedly.

The sad shortage of physicians in Great Britain emphasizes the need of wise procedure on our part to forestall a similar situation arising in this country in the future. It can be averted by preventing the drafting for military training of medical students in approved medical schools and interns in approved hospitals.

On behalf of The New York Academy of Medicine, I beg to submit to you a resolution bearing on this subject. This resolution is being sent to the Secretary of War and the Secretary of the Navy as well as to the Surgeons-General of our Armed Forces and to General Hershey.

I realize that this is a detail in comparison with the many important issues now before you, but a detail of such importance that I do not feel hesitant to bring it to your attention.

The text of the resolution follows:

An adequate supply of well-trained physicians is essential for National Defense as well as for the safety of the civil population. To-day there is greater need than ever before for the maintenance of full student quotas in all our medical schools and for the selection of the best qualified candidates for admission to the medical schools. It is likewise essential for the best interests of the country that medical graduates be allowed to complete their basic training as interns in approved hospitals, as without this training they are not qualified to assume the responsibilities of medical practice either in war or peace. The Selective Service authorities must be aware of the serious shortage of trained physicians in some of the belligerent foreign countries because of short-sighted interference with the period of medical training. A similar attitude in this country might have the gravest consequences in the future both for our military forces and our civil establishments.

The New York Academy of Medicine, therefore, urges the Selective Service Administration to give proper con-

sideration to the existing situation through its Local Boards. In making their decisions as to deferment, the Local Boards should inquire whether the students who are matriculated in approved medical schools and the interns who are receiving training for a period not exceeding two years in approved hospitals are pursuing occupations which are essential to "the health, safety, or interest of the nation." In other words, as group deferment of medical students and interns is contrary to the spirit of the Selective Training and Service Act, the decision in each case should be weighed by consideration of national expediency, and for that the Local Boards have the necessary authority and responsibility under the law.

THE AMERICAN PHILOSOPHICAL SOCIETY

At the annual general meeting of the American Philosophical Society held in the Hall of the Society in Philadelphia on April 18, 19 and 20, officers re-elected were: *President*, Roland S. Morris; *Vice-presidents*, Edwin G. Conklin, William E. Lingelbach; *Secretary*, W. F. G. Swann, and *Curator*, Albert P. Brubaker; *Treasurer*, Fidelity-Philadelphia Trust Company. Dr. Frank Aydelotte, president of the Institute for Advanced Study at Princeton, was elected a vice-president and Dr. Benjamin D. Merritt, of the university, was elected one of the secretaries. Members elected to the council to serve for three years were: *Class I*, Herbert E. Ives; *Class II*, Ross G. Harrison; *Class III*, Joseph H. Willits, and *Class IV*, William Bell Dinsmoor.

The following thirty resident and eight foreign members were elected:

Mathematical and Physical Sciences—Class I: Griffith Conrad Evans, professor of mathematics, University of California; Henry Eyring, professor of chemistry, Princeton University; Louis Frederick Fieser, professor of organic chemistry, Harvard University; John Robert Kline, professor of mathematics, University of Pennsylvania; Isidor Isaac Rabi, professor of physics, Columbia University; John Torrence Tate, professor of physics, University of Minnesota; Theodor von Kármán, professor of aeronautics, California Institute of Technology.

Geological and Biological Sciences—Class II: Fay-Cooper Cole, professor of anthropology, University of Chicago; Evarts Ambrose Graham, professor of surgery,

School of Medicine of Washington University; Albert Baird Hastings, Hamilton Kuhn professor of biological chemistry, Harvard Medical School; Walter Samuel Hunter, professor of psychology, Brown University; Charles William Metz, professor of zoology, University of Pennsylvania; William Jacob Robbins, director of the New York Botanical Garden and professor of botany, Columbia University; Lewis John Stadler, professor of field crops, University of Missouri; William Hay Taliaferro, Eliakim H. Moore distinguished service professor of parasitology, University of Chicago.

Social Sciences—Class III: Robert Treat Crane, executive director, Social Science Research Council; Manley Ottmer Hudson, Bemis professor of international law, Harvard University; Lindsay Rogers, Burgess professor of public law, Columbia University; Arthur Meier Schlesinger, Francis Lee Higginson professor of history, Harvard University; Thomas Jefferson Wertenbaker, Edwards professor of American history, Princeton University; Leo Wolman, professor of economics, Columbia University.

Humanities—Class IV: Carl William Blegen, professor of classical archeology, University of Cincinnati; Howard Mumford Jones, professor of English, Harvard University; Alfred Louis Kroeber, professor of anthropology, University of California; Lewis Mumford, America, N. Y.; Marjorie Hope Nicolson, professor of English, Columbia University; Arthur Darby Nock, Frothingham professor of the history of religion, Harvard University; Ephraim Avigdor Speiser, professor of Semitics, University of Pennsylvania.

Council Nominees: Andrew Ellicott Douglass, director of the Steward Observatory, University of Arizona; George William McClelland, provost of the University of Pennsylvania.

Foreign: Ronald Aylmer Fisher, Galton professor of eugenics, University College, London; Ejnar Hertzsprung, director, Leiden Observatory; Theodor Svedberg, professor of physical chemistry, University of Uppsala; August Krogh, professor of zoophysiology, of the University of Copenhagen; Sir D'Arcy Wentworth Thompson, professor of natural history, University of St. Andrews; William E. Rappard, professor of political science, University of Geneva; Harold Idris Bell, honorary reader in papyrology, the University of Oxford; Arnold Joseph Toynbee, research professor of international history, University of London.

SCIENTIFIC NOTES AND NEWS

A BRONZE bust of Dr. Ernest E. Tyzzer, George Fabyan professor of comparative pathology and professor of tropical medicine at the Harvard Medical School, was recently presented to Dr. Tyzzer to be placed in his department in recognition of his long service to the university. Dr. Cecil K. Drinker made the presentation at a luncheon given in his honor.

THE John Scott Medal and the sum of \$1,000, given by the City of Philadelphia for "outstanding

achievement in medical science," has been awarded to Dr. Owen H. Wangensteen, professor of surgery and head of the department of the Medical School of the University of Minnesota, in recognition of his work in the development of a suction siphonage treatment of acute intestinal obstruction.

At the recent meeting in Chicago of the American Institute of Nutrition, the Mead, Johnson and Company prize of \$1,000 for work on the vitamin B com-

plex was awarded to Dr. Roger J. Williams, professor of chemistry at the University of Texas, for his "outstanding work on the isolation and identification of pantothenic acid."

DURING his visit to England Dr. James Bryant Conant, president of Harvard University, was made freeman of Southwark, where John Harvard, founder of the university, was born, in recognition "of his eminent work as president of Harvard; his leadership in the United States of America in the cause of liberty and justice, and the invaluable assistance rendered by him to the British Empire while engaged in defending the cause of freedom."

DR. JAMES EDGAR PAULLIN, professor of clinical medicine at the School of Medicine of Emory University, was chosen president-elect of the American College of Physicians at the recent Boston meeting. He will succeed as president next year Dr. Roger I. Lee, who was inducted into office at Boston.

OFFICERS of the Michigan Academy of Arts and Letters have been elected as follows: *President*, Dr. Irving D. Scott; *Secretary*, Dr. Harry W. Hann; *Treasurer*, Dr. Mischa Titiev; *Editor*, Dr. William C. Steere; *Librarian*, Dr. W. W. Bishop, all of the University of Michigan. Professor Edward C. Prophet, of Michigan State College, has been elected *vice-president*.

THE following officers have been elected by the Royal Astronomical Society, London: *President*, Dr. Sydney Chapman, professor of mathematics at the Imperial College, South Kensington; *Vice-presidents*, Dr. David Brunt, professor of meteorology at the Imperial College; Sir James Jeans, professor of astronomy in the Royal Institution; The Rev. T. E. R. Phillips; Henry C. Plummer, professor of mathematics in the Military College of Science, Woolwich; *Treasurer*, J. H. Reynolds, ex-president of the society; *Secretaries*, D. H. Sadler, Dr. A. D. Thackeray; *Foreign Secretary*, Sir Arthur Eddington, Plumian professor of astronomy at the University of Cambridge.

THE retirement from active service is announced of Dr. Horace S. Uhler, professor of physics at Yale University, who has been connected with the university for thirty-four years.

ASSOCIATE PROFESSOR ERNEST GLEN WEAVER has been promoted to a full professorship of psychology at Princeton University.

DR. HARRY S. N. GREENE, of the Rockefeller Institute for Medical Research at Princeton, N. J., has been appointed professor of pathology and surgery at Yale University.

DR. ROBERT D. VOLD, Bristol-Myers post-doctorate

research fellow at Stanford University, has been appointed assistant professor of chemistry at the University of Southern California.

ANTIOCH COLLEGE announces the following changes in the department of chemistry for next year: Professor Austin M. Patterson, having reached the retirement age of sixty-five years, will become professor emeritus, retaining an informal connection with the college; Professor W. A. Hammond is giving up his course in industrial chemistry to devote his time to the manufacture of drierite; Professor C. S. Adams will resume the revolving chairmanship of the department; Dr. Robert N. Boyd is promoted to an assistant professorship, and Calvin Vander Werf, who is about to receive his doctor's degree from the Ohio State University, will become instructor.

THE title of professor of human and comparative anatomy was conferred upon Dr. A. J. E. Cave at a recent meeting of the Royal College of Surgeons, London.

SIR LAWRENCE BRAGG, Cavendish professor of experimental physics at the University of Cambridge, and Dr. Charles Darwin, director of the British National Physical Laboratory, recently left England for Canada. Sir Lawrence will work in Ottawa at the National Research Buildings in cooperation with Professor Fowler as liaison officer with Canadian scientific men. Dr. Darwin will work in Washington.

DR. D. MURRAY ANGEVINE, assistant professor of pathology at the School of Medicine of Cornell University, became on May 1 bacteriologist and pathologist at the Alfred I. du Pont Institute of the Nemours Foundation at Wilmington, Del. Other appointments that have been made recently include Dr. Lee E. Farr, associate in medicine at the Hospital of the Rockefeller Institute for Medical Research, New York City, as director of research and pediatrician-in-chief. He became at the same time visiting associate professor of pediatrics of the School of Medicine of the University of Pennsylvania. Dr. Douglas A. MacFadyen, associate in chemistry, also of the Rockefeller Hospital, was appointed chief of biochemistry, and has become associated with the University of Pennsylvania as visiting assistant professor of pediatrics.

DR. JACQUES ERRERA, Belgian chemist, formerly professor of physical chemistry at the University of Brussels, has been appointed manager of the Research and Control Division of Sidney Blumenthal and Company at Shelton, Conn.

DR. WILLIAM M. GERMAN, pathologist at the Good Samaritan Hospital, Cincinnati, sailed from New York on April 11 to conduct a three months' course in pathology at the University of Bogota, Colombia.

PROFESSOR L. G. ALLBAUGH, of the department of economics of Iowa State College, has been granted leave of absence for fifteen months. During this period he will be chief of the Section of Farm Management of the Farm Security Administration at Washington.

THE Christian A. Herter Lectures of the New York University College of Medicine were delivered on April 22 and 23 by Dr. Michael Heidelberger, associate professor of biochemistry at the College of Physicians and Surgeons, Columbia University. The subject of the lectures was: "Immunochemistry."

THE Edgar Fahs Smith Memorial Lecture of the department of chemistry and chemical engineering of the University of Pennsylvania will be delivered on the evening of May 23 by Dr. Arthur A. Blanchard, professor of inorganic chemistry at the Massachusetts Institute of Technology. He will speak on "The Metal Carbonyls."

DR. H. I. SCHLESINGER, professor of chemistry at the University of Chicago, will deliver on May 9 the John Howard Appleton lecture at Brown University on "New Developments in the Chemistry of the Hydrides of Boron." This is the second lecture in the series for the year 1940-41.

DR. OSCAR RIDDLE, of the department of genetics at Cold Spring Harbor, N. Y., of the Carnegie Institution of Washington, lectured on April 24 at the New York Academy of Medicine. His lecture was entitled "The Promise of Endocrinology."

THE Honors Day address of the New York State Veterinary College at Cornell University was given on the evening of March 17 by Dr. Thomas M. Rivers, director of the hospital of the Rockefeller Institute for Medical Research, New York City, who spoke on "The Romance of Viruses." This address was given at the annual dinner of the Cornell Junior Chapter of the American Veterinary Medical Association, an undergraduate organization. The prizes for the year which had been awarded by the faculty of the college were presented by the dean of the university faculty, Dr. Cornelius Betten.

DR. HAROLD G. MOULTON, president of the Brookings Institution, Washington, D. C., will give the Graduate School Convocation address at Brown University on June 14. His subject will be "Changing Economic Conditions."

A SYMPOSIUM of invited papers on nuclear energy sources in stars will be held on May 3 at the Washington meeting of the American Physical Society, under the sponsorship of Dr. George Gamow, professor of theoretical physics at the George Washington University, who will open and close the discussion. Other

speakers will be Drs. Hans A. Bethe, Edward Teller, R. E. Marshak and C. L. Critchfield.

BECAUSE of the urgent need for qualified persons to fill engineering positions in the National Defense program, the Civil Service Commission has found it necessary to announce a new engineer examination which includes all fields of engineering except chemical, metallurgical, marine and naval architecture. It is important that engineers know of the modified requirements of the new examination. The principal change from previous engineer examinations is the allowing of complete substitution of qualifying experience for the education lacking. Also, the age limit has been raised to sixty years.

THE eighth annual Metal Mining Convention and Exposition will be held at the Fairmont Hotel, San Francisco, from September 29 to October 2. A statement made by Julian D. Conover, secretary of the congress, reads: "This convention is of greater importance than ever before, coming, as it does, in the midst of the mining industry's strenuous effort to supply the basic sinews of national defense. The meeting will afford an opportunity to discuss the many new problems which have arisen in this critical period, to co-ordinate efforts for efficient maximum production, and to work out further plans for full cooperation in the defense program. Of special significance will be the manufacturers' exhibits of the latest developments in machinery and equipment to aid in present-day production problems."

At the three hundred and fifth meeting of the Washington Academy of Sciences on April 17 there was given a series of illustrated reports on various phases of the 1940 South American eclipse expedition sponsored by the National Geographic Society and the National Bureau of Standards. They were as follows: "The 1940 National Geographic Society—National Bureau of Standards Eclipse Expedition," by Irvine C. Gardner, National Bureau of Standards; "A Photographic Determination of the Time of Contact during a Total Solar Eclipse," by Paul A. McNally, S.J., Georgetown University; "The 1940 Flash Spectrum," by Carl C. Kiess, National Bureau of Standards; "Sky Brightness at Patos, Brazil, 1940," by Edward O. Hulburt, U. S. Naval Research Laboratory, and "Ionosphere Observations at the 1940 Eclipse," by Theodore R. Gilliland, National Bureau of Standards.

THE Zoological Society of San Diego announces that the trustees of the Ellen B. Scripps Foundation have allocated funds for the renewal of the two research fellowships initiated at the Biological Research Institute. The fellowships pay \$1,000 per annum for the pursuit of research on a full-time basis on some phase of animal biology. Since the Biological Re-

search Institute is not directly affiliated with any university, it is desirable that a recipient of a fellowship work under the department from which he applies. Only the thesis or dissertation requirements or parts thereof can be fulfilled at the Biological Research Institute. Preference will be given to advanced graduate students or those already having the degree of doctor of philosophy. Applications should be addressed to Dr. Charles R. Schroeder, Biological Research Institute, Balboa Park, San Diego, California, before May 15, 1941.

THE greater part of the Agricultural Engineering Building at Iowa State College was destroyed by fire on March 31. Much equipment was lost, but most of the records were saved. The Iowa General Assembly has appropriated \$125,000 for the replacement of the building.

ALPHA EPSILON DELTA, the national honorary pre-medical fraternity, installed its thirty-second chapter at the University of Detroit on March 8, when the Iota chapter of the Omega Beta Pi fraternity became the Michigan Alpha chapter with the induction of twenty students and two faculty members. Honorary members of the charter group are Professor Leo E. Buss, department of biology, and Dr. Robert C. Page, assistant medical director of the Standard Oil Company of New Jersey, who was formerly the national secretary of Omega Beta Pi. The installation dinner was held at the Webster Hall Hotel, with Dr. Maurice L. Moore, of the Medical Research Division of Sharp and Dohme, who is national secretary of the fraternity, as the installing officer. Following the dinner, Father John F. Quinn, dean of the College of Arts and Sciences of the University of Detroit, welcomed Alpha Epsilon Delta to the university and spoke on the problems of pre-medical education.

At the request of the editors of *Nutrition Ab-*

stracts and Reviews, the American Institute of Nutrition has agreed to assume responsible leadership in the direction of continuing unbroken the service rendered by the journal. This involves the abstracting of pertinent material in European and other scientific journals which are not available in Great Britain at the present time. The list includes more than two hundred technological and scientific periodicals. Dr. Arthur H. Smith, of the College of Medicine of Wayne University, will act as the American editor and members of the American Institute of Nutrition, as well as others who are interested, will be asked to assist in preparing the abstracts.

THE centenary of the Royal Botanic Gardens, Kew, as a government institution occurred on April 1. The first director, Sir William Hooker, took office on April 1, 1841. The gardens had previously been the private property of the royal family. To mark the centenary the present director, Sir Arthur Hill, read a paper before the Linnean Society on April 3, giving an account of the work of the gardens during the last century.

ACCORDING to *Nature*, the Advisory Research Council of the British Chemical Society, in collaboration with the Association of British Chemical Manufacturers, is putting into operation a scheme for organizing the preparation of fine chemicals in Great Britain by part-time volunteer workers in the laboratories of universities, technical colleges and other institutions. Compounds so prepared must be required for work of national importance and be not available commercially, and the manufacturers of fine chemicals are themselves unable, or do not find it convenient, to meet the demands. It is intended that preparations should be carried out on a cost-price basis, which would include charges for materials, gas, electricity, etc., but not for the workers' services. No profits of any kind will be permitted.

DISCUSSION

THE RATE OF PERFORMANCE OF OSMOTIC WORK ON THE CHLORIDE ION DURING ACTIVE INTESTINAL ABSORPTION

THE rate of performance of osmotic work on the chloride ion during active intestinal absorption of chloride is given approximately by the equation,

$$dW/dt = (dn/dt)RT \ln(C_p/C), \quad (1)$$

where dW/dt is the rate of osmotic work, dn/dt the number of mols of chloride transferred from the intestinal lumen to the blood in unit time, R the gas constant, T the absolute temperature, C_p the plasma chloride concentration in M./l., and C the concentration of chloride in the intestinal lumen in M./l. If V is the volume of fluid in the intestine, $dn/dt = -d(CV)/dt$ and

$$dW/dt = -[d(CV)/dt]RT \ln(C_p/C). \quad (2)$$

Using the equations of Peters and Visscher¹ empirically to describe the course of active absorption under their conditions, we have

$$CV = C_0 V_0 (V/V_0)^{R_0/D}, \quad (3)$$

$$\text{and } V = V_0 - Dt, \quad (4)$$

where C_0 and V_0 are original values for concentration and volume, t time, and R_0 and D constants. From equations (3) and (4),

$$d(CV)/dt = -CR_0. \quad (5)$$

¹ H. C. Peters and M. B. Visscher, *Jour. Cell. and Comp. Physiol.*, 13: 51, 1939.

Substituting in equation (2),

$$dW/dt = CR_oRT \ln(C_p/C). \quad (6)$$

Applying equations (3), (4) and (6) to experiment 2 of Ingraham, Peters and Visscher,² we obtain Fig. 1, which illustrates in a general way the osmotic work

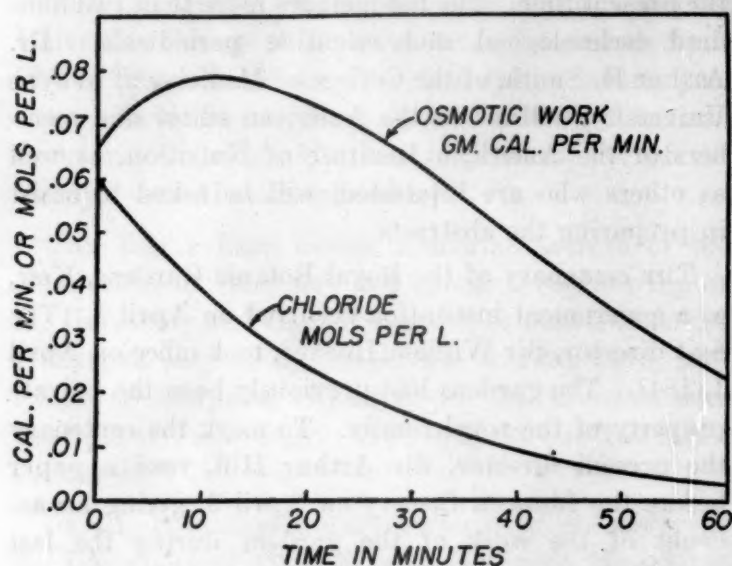


FIG. 1. Rate of performance of osmotic work on the chloride ion and chloride concentration during active absorption.

and concentration curves obtained in this type of experiment.

Differentiating equation (6) with respect to C and equating to 0, we find that dW/dt reaches a maximum when $C = 0.367 C_p$. Since, in the dog, C_p is generally close to 0.100, we can substitute $C_p = 0.100$ and $C = 0.0367$ in equation (6) and obtain as an approximate equation for the maximum rate of osmotic work during an experiment,

$$(dW/dt)_{\max} = .023R_o, \quad (7)$$

where R_o is in cc per min. and $(dW/dt)_{\max}$ in cal. per min.

Values of $(dW/dt)_{\max}$, calculated from the available data and expressed as cal. per min. per cm of intestine, are given in Table I. Since $(dW/dt)_{\max}$ is

TABLE I
MAXIMUM RATE OF OSMOTIC WORK ON THE CHLORIDE ION DURING ACTIVE ABSORPTION

Experimental data	Type of exp.	$(dW/dt)_{\max}$ cal. per min. per cm
Ingraham et al. ² 3 expts., 3 dogs	Acute	0.0009, 0.0013, * 0.0016 Average, 0.0013
Peters and Visscher ¹ 9 expts., 9 dogs	Acute	0.0007, 0.0010, 0.0011, 0.0012, 0.0012, 0.0015, 0.0018, 0.0019, 0.0020 Average, 0.0014
Dennis and Visscher ³ 6 expts., 2 dogs	Chronic loop	0.0013, from average curve, Figs. 1a and 1b

* Exp. 2, described more completely in Fig. 1.

² R. C. Ingraham, H. C. Peters and M. B. Visscher, *Jour. Phys. Chem.*, 42: 141, 1938.

³ C. Dennis and M. B. Visscher, *Am. Jour. Physiol.*, 131: 402, 1940.

the maximum value of the minimum power requirement, its calculation may be of value in finding the mechanism of active chloride absorption. Any proposed mechanism must furnish, at a suitable time during the course of an average experiment of the type considered here, at least 0.0013 gram cal. per min. per cm of intestine before it can reasonably be regarded as a possible sole source of the necessary energy.

H. C. PETERS

UNIVERSITY OF TENNESSEE

THE MOUSE ANTIALOPECIA FACTOR

WOOLLEY¹ described a syndrome produced in mice on a synthetic diet containing thiamine, riboflavin, nicotinic acid, pyridoxin, β -alanine, pantothenic acid and choline. The symptomatology as described was one in which the hair on the entire body excepting the head and tail falls out, leaving the trunk naked. The denuded areas showed a reddening, and sores developed. Woolley² identified this factor as inositol or phytin. Norris and Hauschildt³ reported the development of somewhat similar lesions on a diet deficient in pantothenic acid and inositol.

Using a basic diet of casein, 18; sucrose, 67; salts, 4; cod liver oil, 2, and butter fat, 9, supplemented with 20 ug. of thiamine, 15 ug. of riboflavin, 10 ug. of pyridoxine, 0.5 mg. of nicotinic acid, 1.0 mg. of choline, 10 ug. of pantothenic acid and 50 ug. of β -alanine, we noted after six weeks a slight loss of hair on the back, and some graying. On the same basic diet with the same supplements, but with added inositol at 250 ug. daily, we noted exactly the same symptoms. Following both groups of 100 mice each for three months, no differences were observed. Thus, we have been unable to detect any effect from added inositol.

Using the Norris and Hauschildt diet, which is deficient in both inositol and pantothenic acid, we observed in 100 mice all the symptomatology reported by these workers, but immediate responses are observed to 150 ug. of pantothenic acid daily.

The mouse on a diet including thiamine, riboflavin, nicotinic acid, β -alanine, pyridoxin, pantothenic acid, choline and inositol responds to Labco Rice Polish Factor II, at 250 mg. daily.

It is suggested that the discrepancies observed are due to genus variation, imbalance of vitamin B complex members or altered intestinal bacterial flora. Under our experimental conditions, inositol has no effect on the nutrition of the Rockland strain black mouse. Furthermore, pantothenic acid, while curing the skin lesions described by Norris and Hauschildt³

¹ D. W. Woolley, *Jour. Biol. Chem.*, 136: 113, 1940.

² D. W. Woolley, *SCIENCE*, 92: 384, 1940.

³ E. R. Norris and J. Hauschildt, *SCIENCE*, 92: 316, 1940.

does not completely cure the graying of the fur, which responds to Labco Rice Polish Factor II. It is to be emphasized that we used black mice, whereas Woolley used white albino mice. Our results agree with those implied by György and Poling⁴ to be published.

GUSTAV J. MARTIN

WARNER INSTITUTE FOR THERAPEUTIC RESEARCH,
NEW YORK

NEED FOR THE PRESERVATION OF NATURAL AREAS EXEMPLIFYING VEGETATION TYPES

THE communication on this subject by Dr. Henry I. Baldwin in *SCIENCE* for January 24, 1941, should arouse not only ecologists but all interested in natural history, whether merely amateurs or people seriously engaged in botanical or zoological work.

Dr. Baldwin, in concluding his statement, says that "until data are circulated on (a) what vegetation types (and animal communities) are at present adequately represented in protected areas and (b) what other types should be so protected . . . we shall go on setting aside reserves in hit-or-miss fashion, duplicating some excessively and overlooking others until it is too late."

It must certainly be admitted that we have been acting not merely in the "hit-or-miss" fashion that Dr. Baldwin warns against, but with especial emphasis on the "miss" part of the alternative. We have secured really enormous reservations of the least important kinds—high mountain areas—because they are of no commercial value and nobody objects much, and we have as a rule failed entirely to protect examples of the most important of all kinds of areas and those which are disappearing most rapidly. These are the last and rapidly vanishing remnants of the various types of primeval forest.

The U. S. Forest Service, which alone has the power and opportunity to give us such reservations on any considerable scale, has persistently failed to recognize this obligation to the American public.

The so-called "primitive areas," "roadless areas," "recreation areas," etc., which the Forest Service has established had first to pass a searching test for absolute commercial worthlessness before selection. Naturally, they consist almost entirely of high, rocky, barren, nearly or quite treeless areas, which are inhospitable to most forms of plant and animal life, and which were safe from exploitation anyway because nothing exists there to exploit. Were they made wild life sanctuaries, that would be one thing to be thankful for, but they are nothing of the kind. Quite the opposite.

⁴ Paul György and C. E. Poling, *Proc. Soc. Exp. Biol. and Med.*, 45. 773, 1940.

Those interested in the ecological side of zoology and botany or in the preservation of areas of especial scenic, geological or other scientific interest should wake up to the fact that of the vast extent of our immense country the national parks are the only areas required by law to be kept in a natural state.

This is not an ideal state of things, for the protection of the national parks can not be as complete as it should be, owing to the necessities of providing for the tourist traffic. The parks consist also in too large proportion of high mountain areas, and their extent of fine primeval forest with trees of any considerable size is far less than commonly supposed, yet they contain all we have of undisturbed nature that has any prospect of surviving. The National Park Service realizes this and tries to protect the natural plant and animal life and scenery of the parks.

There are still on government-owned lands at least three or four more considerable areas of outstanding scenic and scientific interest in urgent need of protection. Only by making them national parks can we save them.

Some of the existing parks also need to be enlarged in order to serve their purpose properly. For instance, a number of them are composed so nearly exclusively of high-altitude areas that they can not provide winter range for the large mammals that they are supposed to protect. We need also to safely protect as "national monuments" a number of most interesting localities of too small area for national parks.

Thirty years' experience shows that no action toward fulfilling the requirement of the nation which Dr. Baldwin's letter pointed out can be expected from any government bureau we have now, or have any prospect of having under a government constituted as ours is, except the National Park Service.

Heartily as we may agree with Dr. Baldwin in regard to the need of more land reservations for scientific purposes, we must dissent from his assertion that the first thing to do is to spend a matter of years in an "inventory" of desirable areas. The most important natural areas and the most immediately threatened ones are well known now. What we need is action before it is too late.

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RESEARCH IN TROPICAL AMERICA

BARRO COLORADO ISLAND in the Canal Zone was set aside as a reserve for biological study and its preservation has recently been assured by Act of Congress. In a recent visit there we were able to secure two-toed and three-toed sloths, armadillos, anteaters and iguanas in abundance and in good condition for studies of their respiratory metabolism. These animals were

selected because they differ phylogenetically from the animals which have commonly been studied and because the edentate mammals apparently live with a body temperature which is usually lower than that of other mammals. The management of the laboratory is adjusted to receive all the benefits of the various technical and other facilities in the Canal Zone, and the provision of animals was very satisfactory. By careful arrangement in advance we transported all the equipment necessary for our physiological work. We found that we could count upon such essential local supplies as distilled water and ice and some reagents and articles which had been omitted or consumed. The laboratory space and the living arrangements were satisfactory, and it was a great advantage to be able to live and work isolated in the establishment at Barro Colorado Island. The situation was also pleasant and interesting, and the opportunity for observing the rich tropical flora and fauna was especially agreeable to physiologists who are usually confined to the artificial environment of the laboratory.

To many biologists the opportunities in the tropics are quite familiar, but it is not usually realized how great is the opportunity for experimental and com-

parative physiology in the tropical parts of America. Barro Colorado Island by reason of its situation and stable establishment is particularly favorable as a site in which to carry on experimental work, for the living material is there in its natural condition, and by careful planning the means for experimental study can be well provided. It seems likely that with so much of the world now cut off from the view of American biologists they will turn more particularly to the American tropics in order to extend their range of study and reduce the deadening influence which isolation will certainly bring. In tropical America the emphasis will be largely upon the new animals and plants and new environments rather than upon the personal element of association with large groups of scientists. Among the institutions of Central and South America there are, however, ancient cultural institutions, and many are carrying on scholarly work which pertains to the country in which they live. By travel among those countries, American biologists working among the scholars of Central and South America will find friendly interests which will go far toward developing good-will among the different nations of the Americas.

LAURENCE IRVING

SWARTHMORE COLLEGE

SCIENTIFIC BOOKS

RECENT BOOKS ON THE HISTORY OF MEDICINE

- A History of Medicine.* By ARTURO CASTIGLIONI, formerly professor at the University of Padua; research associate in the history of medicine at Yale University. Translated from the Italian and edited by E. B. Krumbhaar. xxvii+1013+xl pp., with 443 illustrations. New York: A. Knopf. 1941. \$8.50.
- Progress in Medicine: A Critical Review of the Last Hundred Years.* By IAGO GALDSTON, with a Foreword by H. E. Sigerist. ix+347+xiv pp. New York: A. Knopf. 1940. \$3.00.
- The Story of Surgery.* By HARVEY GRAHAM. xv+425 pp., with 23 illustrations. New York: Doubleday, Doran and Company, Inc. 1939. \$3.75.
- Medical Work of the Knights Hospitallers of Saint John of Jerusalem.* By EDGAR ERSKINE HUME, lieutenant-colonel, Medical Corps, United States Army. xv+371 pp., with 130 illustrations. Baltimore: The Johns Hopkins Press. 1940. \$3.00.
- The Chinese Way in Medicine.* By EDWARD H. HUME. 189 pp., with frontispiece and 8 illustrations. Baltimore: The Johns Hopkins Press. 1940. \$2.25.
- Science and Seizures: New Light on Epilepsy and Migraine.* By WILLIAM GORDON LENOX, president,

- International League against Epilepsy. xiii+258 pp. with 10 illustrations. New York: Paul B. Hoeber (Harper and Brothers). 1941. \$2.50.
- Observations Made During the Epidemic of Measles on the Faroe Islands in the Year 1846.* By PETER LUDWIG PANUM. Trans. by A. S. HATCHER, with Memoir by J. J. PETERSEN (Trans. by J. DIMONT) and Introduction by JAMES ANGUS DOULL. xxxvii+111 pp., with a frontispiece. New York: Delta Omega Society, American Public Health Association. 1940. \$2.50.
- Man on His Nature.* By SIR CHARLES SHERRINGTON. 413 pp. with 12 illustrations. New York and Cambridge: The Macmillan Company and The Cambridge University Press. 1941. \$3.75.
- Medicine and Human Welfare.* By HENRY E. Sigerist, William H. Welch professor of the history of medicine in The Johns Hopkins University. ix+148 pp. + 20 illustrations. New Haven: Yale University Press. 1941. \$2.50.
- Magic in a Bottle.* By MILTON SILVERMAN. xiii+314 pp. New York: The Macmillan Company. 1941. \$2.50.
- Plague on Us.* By GEDDES SMITH. 365 pp., with 11 (unlisted) illustrations. New York: The Commonwealth Fund. 1941. \$3.00.
- De Morbis Artificum Bernardini Ramazzini Diatriba:*

Diseases of Workers. By WILMER CAVE WRIGHT, professor of Greek in Bryn Mawr College. The Latin Text of 1713 Revised, with translations and notes. xlvii+549 pp., with 3 illustrations. Chicago: The University of Chicago Press. 1940. \$5.00.

IN his preface to Dr. Galdston's book, Professor H. E. Sigerist, of The Johns Hopkins University Institute of the History of Medicine, offers a casual exaggeration. "In recent years we have been presented with an infinity of popular medical books that you can not read without nausea. I never touch a book that is called *The Romance of . . .*, or *The Story of . . .* Paul de Kruif has created the genre in medical historiography at which he is a master, but his many imitators have failed miserably." This comment emphatically does not apply to the volumes here under consideration.

Castiglioni's "History of Medicine" first appeared in 1927. It has been skilfully translated and edited by Dr. Krumbhaar, and offers a fresh and original survey of the applications of scientific development to the broad problem of disease. With admirable and extensive illustrations it emphasizes the contributions of middle Europe to medicine. The discussion of Graeco-Roman medicine is particularly thorough. While Castiglioni's volume is not as detailed nor as inspiring as Garrison's well-known work (4th edition, Phila., 1929), it will probably supplant Garrison as a standard English reference in the history of medicine, since it is unlikely that a revision of Garrison would be successful even if undertaken by the brilliant editors who were his associates at Johns Hopkins.

Dr. Galdston's description of major developments in medicine during the last hundred years is stimulating but highly selective. It emphasizes particularly the development of bacteriology and its application in the prevention and treatment of disease, revolutionary studies in nutrition and endocrinology, and the startling growth of systematic psychiatry. As Dr. Galdston emphasizes, the latter may be medicine's most significant philosophical contribution to society, since it affords a basis for knowing ourselves.

Harvey Graham is the pseudonym of a well-known British surgeon. He has ably organized a broad historical account of his specialty. Surgery was born, he says, of a queer muddle of demonology, tribal ritual and social necessity. Much of its basic technique is amazingly ancient. Its great success has been due to the skill with which accumulating scientific knowledge has been applied to its problems by a host of brilliant thinkers and technicians. In the past century it has expanded widely as a result of the development of anesthesia, asepsis and transfusion. While this history is written with the customary bril-

liant British bias, it suffers from many errors of omission. Transfusion and management of shock, as important factors in the success of modern surgery, are only incidentally mentioned in a penetrating glimpse into the future of surgery.

Colonel Hume's survey of the medical work of the Knights of Saint John is informative and detailed. Founded in the eleventh century, the order is particularly identified with the occupation of Malta (1530) and the establishment of hospitals in various portions of the Mediterranean area and Europe. In addition to its broad humanitarian interest and its careful preparation for the care of the sick, the order was a pioneer in developing military medicine.

Dr. Edward Hume's volume comprises a series of interesting lectures presented at the Institute of the History of Medicine of The Johns Hopkins Medical School. His succinct account of native Chinese medicine is largely a description of an attitude. He refers to the vast formalized medical traditions of China as a record of man's loyalty to ancient beliefs and passive resistance to adversities in his environment. Dr. Hume describes a portion of a large-scale racial experiment in biological adaptation. He points the difference between the Chinese and Westerners, when he says a Chinaman faces his foes, whether human or the forces of nature, with adaptation and compromise, rather than with analytical inquiry with a view to control and transformation.

Dr. Lenox's book represents the culmination of his 20-year effort to further intelligent cooperation between patients, physicians and the public with respect to epilepsy and migraine. With an appropriate historical background, it describes simply and clearly the development of our still meager information and methods of handling these important disorders. This brief inspirational volume is a model of honest treatment of a medical condition for the benefit of sufferers from it.

The translation of Panum's "Observations on Measles" is the third of a series of republications of public health classics made possible by the Delta Omega Society. This is a particularly valuable one in illustrating the method by which epidemiological information can be obtained. Panum (1820-1885) was distinguished for his work in experimental biology at Kiel and at Copenhagen. He was a remarkable general physiologist, and was influential in developing the Scandinavian tradition in this field. His survey of measles in the Faroes was his doctoral dissertation.

Like Panum's volume, "Plague on Us" is dedicated to the memory of Wade Hampton Frost (1880-1938), who did so much to develop scientific interest in epidemiology in this country. Geddes Smith has pre-

pared a superb model of what a popularized historical work relating to science should be. It is clearly and entertainingly written, beautifully organized and illustrated, and so judicious and well documented as to constitute a valuable reference work for specialists in the field. It deals with the history of the great pestilences of bubonic plague, sweating sickness, yellow fever, cholera and influenza. It describes the history of scientific analysis of infectious disease and factors in their control. It offers many cleverly devised scientific detective stories relating to epidemics. It suggests how very much remains to be done in epidemiology and proposes stimulating ways by which these future tasks may be approached.

Appropriate to a notice of these books is a timely volume which is to appear this spring under the auspices of the Commonwealth Fund, "Papers of Wade Hampton Frost, M.D.: A Contribution to Epidemiological Methods," edited by K. F. Maxcy. This volume includes 19 papers prepared by Frost as an officer of the U. S. Public Health Service, and as professor of epidemiology at The Johns Hopkins University School of Hygiene and Public Health. They deal with the principles of epidemiology, the study and control of epidemics and with detail involving the epidemiology of influenza, diphtheria and other important diseases.

Dean of English physiologists, Nobel Laureate in 1932 and sensitive poet, Sir Charles Sherrington weaves into his Gifford Lectures all the strong and brilliant threads of his knowledge and artistry to make a panoramic and awesome tapestry of philosophy. Searching for a suitable text to represent the origin of modernity in the Renaissance, Sir Charles selects "De Abditis Rerum Causis" (Paris, 1548) by Jean Fernel (1497-1558), who was physician to Henry II of France. Fernel's dive into philosophy from the springboard of physiology was prompted by the Hippocratic aphorism asking "Whether in disease there is not something supernatural." To this question the Hippocratic school had answered in the negative in the famous treatise, "On the Sacred Disease." With great sympathy Sir Charles describes Fernel's sophisticated "vitalism" and then proceeds with a masterful accumulation of specific data and logical interpretation to show that no longer is the distinction between living and non-living a qualitative one. With skilful dialectic Sir Charles shows that our current philosophical position is as far beyond that of the Renaissance as is our more commonly appreciated advance of demonstrable knowledge of ourselves and our environment. Or is it?

The goal of biology, to explain living processes in terms of atomic physics, seems to Sir Charles to be vaguely visible as the mists of our ignorance gradually

dissolve. However, his careful and systematic analysis of the vast accumulation of knowledge in his own special field of neurophysiology brings him back to the more fundamental problem of the apparent dualism of the Ego and the Non-Ego, which he calls "mind" and "energy." So far, says Sir Charles, "mind refuses to be energy, just as it always refused to be matter." He insists on differentiating the mental process from the cerebral process, although he admits their approximation.

There on one side electrical potentials with thermal and chemical action, compose a physiological entity held together by energy relations; on the other a suite of mental experience, an activity no doubt; but in what, if any, relation to energy! . . . Our two concepts, space-time sensible energy, and insensible unextended mind, stand as in some way coupled together, but theory has nothing to submit as to how they can be so. Practical life assumes that they are so and on that assumption meets situation after situation; yet has no answer for the basal dilemma of how the two cohere. There is no more of course than mere analogy between this mind-energy complex which teases biology and that other the wave-particle dilemma which has been teasing physics. . . . Naked mind and the perceived world . . . have this in common—they are both concepts; they both of them are parts of knowledge of one mind. They are therefore distinguished, but are not sundered.

Sir Charles shows how science in shedding "anthropisms" becomes behavioristic, but how man through evolution becomes social and more than comprehensible by scientific criteria alone. Man's values for truth may be supplied by natural science, but for values in beauty and goodness man still relies on natural religion, which also values truth.

Natural Religion has not forgone emotion. It has simply taken for itself new ground of emotion, under impulse from and in sacrifice to that one of its 'values,' Truth. Its view of the world and of itself is based upon the purview of what by its light it can accept as true. In that way, for it, much that is comfortable in other religions lapses. If you will, man's situation is left bleaker. One feature of that situation is that the human mind, such as it is, is left the crown of mind to which human life in all its needs has direct access. Compared with a situation where the human mind beset with its perplexities had higher mind and higher personality than itself to lean on and to seek counsel from, this other situation where it has no appeal and no resort for help to beyond itself, has, we may think, an element of enhanced tragedy and pathos. To set against that, it is a situation which transforms the human spirit's task, almost beyond recognition, to one of loftier responsibility. It elevates that spirit to the position of protagonist of a virility and dignity which otherwise the human figure could not possess. It raises the lowliest human being conjointly with the highest, Prometheus-like, to a rank of obligation and pathos which neither Moses in his law-giving nor Job in all his suffering

could present. We have, because human, an inalienable prerogative of responsibility which we cannot devolve, no, not as once was thought, even upon the stars. We can share it only with each other.

One must contemplate Sir Charles's masterpiece from a little distance, so as not to be blinded by its dazzling detail. It is a magnificent artistic achievement, like a great fresco, a grand symphony, or an heroic poem or drama. Considered reflectively, Sir Charles's great effort looms like a peak in the range of the twentieth century Georgians, like a lofty take-off for the flight of current thought.

Dr. Sigerist's "Medicine and Human Welfare" comprises the sixteenth series of "Lectures on Religion in the light of Science and Philosophy" delivered on the Dwight Harrington Terry Foundation at Yale University. In analyzing the manifold relations between medicine and human welfare, Dr. Sigerist organizes his ideas around the concepts of disease, health and the physician. As one aspect of the age-old struggle between man and nature, medicine originated in close association with religion and developed with magic. Dr. Sigerist traces with admirable illustration the development of ideas regarding disease, particularly with reference to cause, which determines type of management. He then contrasts this skilfully with the growth of our ideal of health from the Greek concept of balance and harmony to the modern notion of "public health." Dr. Sigerist considers the physician from a sociological standpoint. He feels that medicine like education will ultimately become a public service in every civilized country.

"Magic in a Bottle" is the first attempt to popularize significant episodes in the development of pharmacology, which occurred only during the last century and a half. Written by an experienced journalist who is a contributing scientist in his own right, it is brilliantly written, highly informative and essentially accurate, even though it may include obviously fictitious conversation for dramatic effect. Selected references offer a trained pharmacologist an opportunity to become acquainted with many of the classics in the science, of which he may not be fully aware. The reader is offered significant detail in the long history of the isolation of biologically active compounds from various crude sources that may have been used as drugs on an empirical basis from antiquity. This effort began with Sertuerner's isolation of morphine from opium in 1803, and includes subsequent isolation and identification of alkaloids, glucosides, vitamins and hormones. Clear and interesting accounts are given of Ehrlich's systematic establishment of chemotherapy, the contributions of Fischer, and the remarkable current work on the sulfanilamides. The volume has been prepared with a rare sense of humor

and with a keen appreciation of the human character of the scientists involved, their struggles, disappointments, lucky breaks, tragedies and enduring achievements.

One of the most important practical developments of modern medicine has been in the field of industrial hygiene. One of the pioneers in this effort was Bernardino Ramazzini (1633-1714), whose treatise on occupational diseases, "De Morbis Artificum," was first published in 1700. Mrs. Wright, professor emeritus of Greek at Bryn Mawr, has prepared a clear translation of this important work, with an unusually stimulating and informative historical introduction. Already in debt to Mrs. Wright for her splendid translation and account of Fracastoro on "Contagion," medical historians must now again acknowledge how much they may owe to a sound classical scholar sympathetic with their problems. Not only is Mrs. Wright's work significant in medical history, and indispensable in a historical survey of occupational diseases, but it also affords a detailed historical picture of the vivid life of a great Italian city in the late seventeenth century. Rendering into current idiom many of the great medical and scientific classics of the Renaissance may do much to give modern scientists a clearer appreciation of the factors that make their science possible. Here is a useful opportunity for classical scholars.

Historical surveys of scientific achievements remain among the most important tasks to which all scientists may contribute. They offer perhaps the best way by which the spirit and method and aim of science can be communicated to the mass of people. George Sarton has frequently indicated the potential significance of such efforts. Wide public appreciation of the spirit and aim of science may be the salvation of our democratic civilization with which the scientific spirit is so closely related. Demonstrable knowledge of ourselves and our environment, voluntarily accepted after critical examination, provides the firm foundation for a rational faith which no arbitrary authority or superstitious ideology may demolish—the solid rock from which free peoples may decide toward what goals they may be able to work, and by what means they may be able to reach them. This knowledge, which is science, must be made fully available to all people, if democracy is to survive. Simply written but thought-provoking and essentially accurate popularizations of science, such as have been so successful in regard to medicine, offer a relatively easy way to obtain public understanding of science, without burdening the citizenry with non-essential, tiresome, technical details. This is their justification, no matter what their stylistic faults.

CHAUNCEY D. LEAKE

SPECIAL ARTICLES

ACETYL AND PHENYLUREIDO DERIVATIVES OF TOBACCO MOSAIC VIRUS

A STUDY of the relationship of chemical structure to biological activity possesses a unique interest in the case of viruses since, when a virus derivative is active, the nature of the virus produced in the host cells on inoculation of the derivative may be determined. If, subsequent to inoculation and multiplication, the virus derivative could be reisolated from the host, evidence would be afforded that the infecting molecules served as more or less exact patterns for the building up of other virus molecules. Furthermore, it might be expected that there would be a difference in the disease produced by such an altered virus, for it is well known that the nature of the disease varies with the strain of the virus. It has been shown that strains of a virus differ in their chemical properties,¹ and recently definite information concerning some of the structural differences that exist between strains of tobacco mosaic virus was obtained.² The possibility exists, therefore, that one might cause structural changes *in vitro* which would, in effect, correspond to the mutation of a virus. If, on the other hand, the inoculation of the virus derivative resulted in the production of normal or unaltered virus, it might be concluded that the structural change was reversed within the cells of the host or that that portion of the molecule involved in the structural change was unimportant and played a subordinate role in the reaction of virus reproduction.

It was shown recently that the sulfhydryl groups of tobacco mosaic virus could be oxidized with iodine without changing the specific virus activity, but that inoculation of the oxidized virus was followed by the production of normal virus.³ Schramm and Müller⁴ reported that the amino groups of tobacco mosaic virus could be completely covered by treatment with ketene or phenyl isocyanate without a decrease in specific virus activity, but it was not determined whether these derivatives could be propagated as such in susceptible hosts. In the present study, which was begun before this work came to our notice, it was not possible to secure complete coverage of the amino groups without a decrease in virus activity, but it was established that derivatives of unchanged specific activity, yet containing about 3,000 substituted groups per molecule of virus, could be prepared. In addition, the nature of the virus produced on inoculation of these derivatives was determined.

In the first experiments, samples of tobacco mosaic virus in 1 M acetate buffer at pH 5.5 were treated with ketene for varying periods of time up to 4 hours. The procedure was adapted from the directions of Herriott and Northrop⁵ and of Li.⁶ In later experiments, it was found that more complete acetylation could be obtained by carrying out the reaction in 0.5 M phosphate buffer at pH 8.1 for separate 1-hour intervals. After each period of acetylation, the virus was dialyzed free of phosphate, isolated by ultracentrifugation, and dissolved in phosphate buffer at pH 8.1 for further acetylation.

The changes in amino nitrogen were followed by the ninhydrin method as applied by Ross and Stanley⁷ and by the Van Slyke manometric method.⁸ It was found that most of the amino groups were acetylated during the first 10 minutes of reaction but that further acetylation proceeded very slowly. According to the ninhydrin test, 50 per cent. of the amino groups were covered during this period. Analyses by the Van Slyke method, however, revealed 70 per cent. acetylation, indicating some lack of specificity in the former method. When the acetylation reaction was carried out at pH 8.1 for periods of 2 and 4 hours, the extent of acetylation of amino groups as determined by the Van Slyke method was increased to 75 and 83 per cent., respectively. The amino nitrogen content of 9 different samples of untreated virus was 0.13 ± 0.01 per cent. The analyses were carried out at 24° C. and digestion with nitrous acid was allowed to proceed for 20 minutes. Under similar conditions, Schramm and Müller obtained the value of 0.25 per cent. amino nitrogen. In addition, they reported negative ninhydrin and Van Slyke tests for their acetylated virus. Since the authors stated that their virus stock was obtained from this laboratory, it is unlikely that the discrepancies can be explained on the basis of different strains of virus.

The decrease in tyrosine plus tryptophane groups due to acetylation was determined colorimetrically by means of Folin's phenol reagent, applied to the unhydrolyzed protein according to the directions of Herriott.⁹ The color changed more slowly with time of acetylation than did the amino nitrogen values, but similarly it also reached a plateau which in this case amounted to a decrease of around 20 per cent. Moreover, the extent of substitution could not be appreci-

¹ W. M. Stanley, *Jour. Biol. Chem.*, 117: 325, 1937.

² C. A. Knight and W. M. Stanley, *Proc. Am. Soc. Biol. Chem.*, *Jour. Biol. Chem.*, 139, lxx, 1941.

³ M. L. Anson and W. M. Stanley, *Jour. Gen. Physiol.*, 24: No. 6, 1941.

⁴ G. Schramm and H. Müller, *Zeits. Physiol. Chem.*, 266: 43, 1940.

⁵ R. M. Herriott and J. H. Northrop, *Jour. Gen. Physiol.*, 18: 35, 1934.

⁶ C. H. Li, *SCIENCE*, 90: 143, 1939.

⁷ A. F. Ross and W. M. Stanley, *Jour. Gen. Physiol.*, 22: 165, 1938.

⁸ J. P. Peters and D. D. Van Slyke, "Quantitative Clinical Chemistry," Vol. II. Williams and Wilkins Company, Baltimore, 1932.

⁹ R. M. Herriott, *Jour. Gen. Physiol.*, 19: 283, 1935.

ably increased by repeated acetylation of the virus. After treatment with NaOH at pH 11, the acetylated virus gave with the Folin reagent 97 per cent. of the color given by a control of untreated virus. In view of Herriott's findings that the chromogenic power of acetylated tyrosine derivatives can be recovered by treatment with alkali, whereas that of acetyl tryptophane can not, it seems probable that a portion of the tyrosine in the virus, but little or none of the tryptophane, was affected by the acetylation.

Tests for biological activity carried out on both *Nicotiana glutinosa* and *Phaseolus vulgaris* plants showed that the specific virus activity of preparations in which 70 per cent. or less of the amino groups were covered was the same as that of the untreated virus. Samples in which the amino groups were 75 to 83 per cent. acetylated showed 25 to 50 per cent. inactivation. A preparation in which the amino groups were covered to the extent of 70 per cent. and the tyrosine plus tryptophane groups to the extent of 20 per cent. was inoculated into a number of young Turkish tobacco plants. The disease produced in these plants was indistinguishable from that in a group of control plants. After a period of 4 to 5 weeks, the viruses were isolated by differential centrifugation. The yields were comparable in the test and control plants. The virus obtained from the plants inoculated with the acetylated virus possessed the normal amino nitrogen content and showed the same chromogenic power towards the Folin reagent as did the virus from the plants infected with normal virus. Further evidence was thus obtained that infecting virus molecules may not necessarily function as exact patterns for reproduction. However, as in the case of the iodine oxidized virus, the objection might be raised that the plant cells had transformed the derivative into the normal form before reproduction occurred. In an effort to obtain a virus derivative less likely to be affected by the plant cells, samples of tobacco mosaic virus in 0.1 M phosphate buffer were treated with an excess of phenyl isocyanate at pH 8 and preparations of phenylureido virus were obtained. The amino groups were 43 to 63 per cent. covered, depending on the time of reaction. The virus derivative showed no significant change in specific virus activity and the disease produced in Turkish tobacco plants was indistinguishable from that caused by ordinary virus. The virus reisolated from the plants possessed the normal amino nitrogen content, in agreement with the results obtained with the acetylated virus.

In order to determine whether the treated preparations were chemically uniform or consisted of molecules altered to widely different degrees, tests were made with the ultracentrifuge and the Tiselius electrophoresis apparatus. The homogeneity of the preparations as determined in the ultracentrifuge was not mea-

surably altered by the two types of chemical treatment. However, because of the nature of the chemical changes involved, a more sensitive test was provided by the electrophoretic mobility. The electrophoresis experiments were carried out at pH 7.3 in 0.1 ionic K_2HPO_4 - KH_2PO_4 -KCl buffer in which 80 per cent. of the ionic strength was provided by the KCl. The acetyl and phenylureido derivatives each possessed mobilities close to -9.3×10^{-5} cm.²/volt sec. as compared with a mobility of -8.3×10^{-5} cm.²/volt sec. for normal virus under the same conditions. It may be seen from the

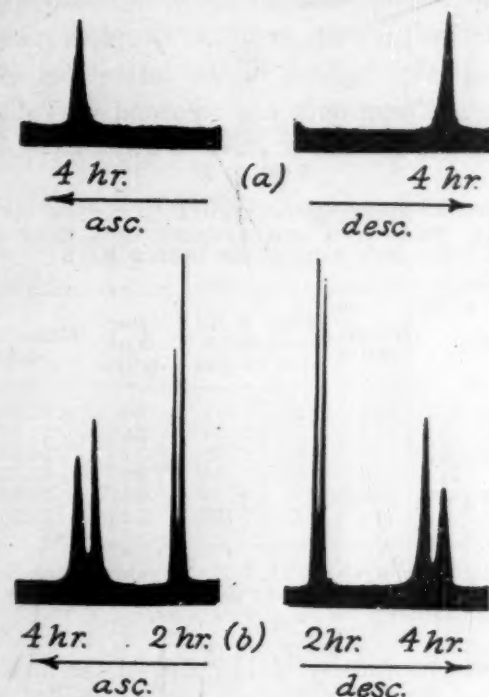


FIG. 1. (a) Acetyl virus. (b) Mixture of normal virus and phenylureido virus.

electrophoresis diagrams presented in Fig. 1 that the derivatives were very homogeneous with respect to electrophoretic mobility and that no detectable amount of the altered proteins migrated with the boundary representing the unchanged virus. In runs made with mixtures prepared with each of the virus derivatives and untreated virus, it was shown that the latter could be separated readily from the derivatives. The results as a whole indicate that the propagation of normal virus did not arise from unchanged virus present in the preparations of the derivatives and demonstrate that a large portion of certain functional groups of the virus molecule may be altered without interfering with the basic reaction of virus reproduction.

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LEUCOCYTE LEVEL AND LONGEVITY IN RATS

PRELIMINARY to a study of the effects of various carcinogenic agents and the growth of induced and

transplanted tumors on the morphology of the blood of rats, a study was made of the variability in the morphology of the blood of normal rats of several closely inbred strains. Among these findings was one of general interest and practical value, especially if it proves to be applicable to man.

It was found that each strain of rats had a characteristic peripheral blood picture. The total leucocyte counts varied from $14.0 \pm .10$ to $25.1 \pm .51$ thousand per cu. mm. Fischer Line 344 rats had the lowest average white cell count and Line 2331 Copenhagen rats had the highest count. The total number of leucocytes and the percentage of neutrophile polys were characteristically highest in the latter and lowest in the former. These data are recorded in Table I and

TABLE I

THE MEAN LEUCOCYTE COUNT AND PERCENTAGE OF NEUTROPHILE POLYS AND THE AVERAGE LIFE SPAN OF SEVERAL STRAINS OF INBRED RATS

Strain	No. of rats	Mean W.B.C. in thousand per cu mm	Per cent. polys	Mean life span days/30
Copenhagen ...	174	$25.1 \pm .51$	38	$19.83 \pm .13$
A x C	228	$17.5 \pm .33$	34	$21.67 \pm .13^*$
August	120	$14.6 \pm .38$	31	$14.03 \pm .04$
Marshall	250	$17.1 \pm .24$	26	$13.53 \pm .09$
Zimmerman ...	287	$15.5 \pm .23$	26	$11.86 \pm .17$
Fischer	719	$14.0 \pm .10$	24	$9.37 \pm .14$

* Based on rats of the first 7 B x S generations and would presumably be somewhat lower for the rats tested which had been inbred another 8 to 10 generations.

represented graphically in Fig. 1. In the final column of the table is recorded the mean life span values in

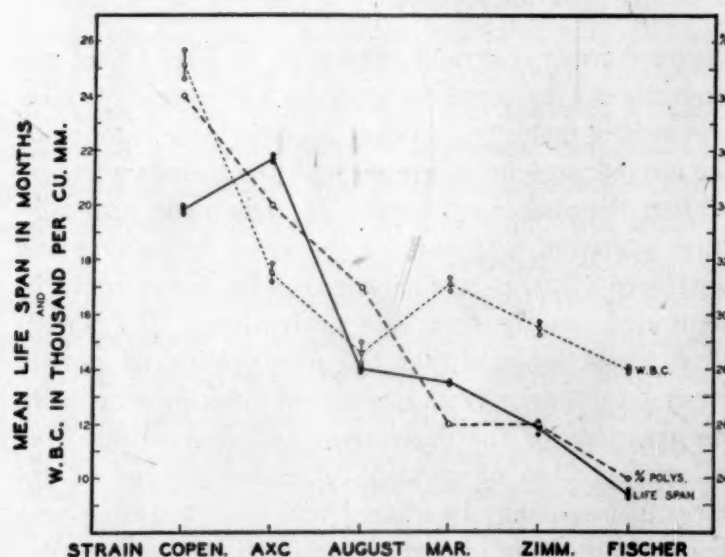


FIG. 1. Shows the relation of the mean total leucocyte count and percentage of neutrophile polys to the average life span in six inbred strains of rats.

months which had been previously determined for rats of these strains.

A parallelism in the observed total number of leucocytes and the relative percentage values of neutrophile polys and the expected average life span is strikingly apparent. Further the females were found to have a

significantly higher leucocyte count than the males (the difference being $0.82 \pm .16$ thousand per cu. mm) and females of most of these strains were previously shown to have significantly longer average life spans than males. This suggests that the association of a relatively high total number of neutrophile polys and a long average life span is probably not accidental.

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ON THE SIZE OF THE LITTER AND THE GESTATION PERIOD OF *PROCAVIA CAPENSIS*

AN article has just come to hand by G. B. Wislocki and O. P. van der Westhuysen on "The Placentation of *Procavia capensis* with a Discussion of the Placental Affinities of the Hyracoidea" (Contributions to Embryology, No. 171, August, 1940). In this article the authors mention that of their eleven specimens of *Procavia capensis* two had six embryos, one four and the others three, two and one embryo. Therefore they regard it as highly probable that *Procavia capensis* carries from one to six embryos. This impression, caused by lack of adequate material, is evidently wrong. As so little is known about the breeding of this animal it may be worth while to give here the data provided by my more abundant material.

The sheep farmers of the Karroo in South Africa have practically exterminated the carnivorous mammals and the large birds of prey that could do harm to their flocks. The result is that the dassie, the natural prey of these predatory animals, has multiplied to such an extent that once I read a short note in a newspaper headed "Dassies like rabbits." That put me on the track and I came in contact with a native professional dassie hunter. The dassies have become so numerous that they are serious food competitors to the sheep and the farmers paid the native a small premium for each dassie. In this way I have collected uteri of *Procavia capensis* over a number of years and have accumulated well over 400 specimens in all stages of development.

The two uteri with six embryos of Wislocki and van der Westhuysen must be very rare exceptions indeed. I have never seen more than four embryos. Most of my material was shared with Professor Nils Holmgren of Stockholm, and in these instances the bicornuate uteri were cut into halves. In my series of entire uteri there are 10 with one embryo, 59 with two, 35 with three and 10 with four embryos. Of the divided, half uteri 179 have one embryo and 62 have two. So we can safely conclude that *Procavia capensis* normally

¹ M. R. Curtis, W. F. Dunning and F. D. Bullock, *Am. Jour. Cancer*, 17: 894, 1933.

carries two or three embryos and sometimes one or four.

Nothing is known about the length of the gestation period of this mammal, as is also stated by Wislocki and van der Westhuysen. All I could find in the literature was that the young are born in November and December. The year I commenced to collect this material I started in the first week of November expecting to find all stages of development in this animal, which is hardly bigger than a rabbit. All fetuses were near birth or the young were already born. The following year I started collecting in August and got embryos about 8 cm. long. The animals caught in May of the

succeeding year possessed already small embryos. It was only in April of the fourth year that I succeeded in obtaining uteri without any outward sign of gravidity. From this we may infer that the length of the gestation period of *Procavia capensis* is six to seven months. This is a very long time for an animal of that size, but Dr. Broom of the Transvaal Museum informs me that the probable ancestors of the dassie were much larger animals, and the length of the gestation period supports that view.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

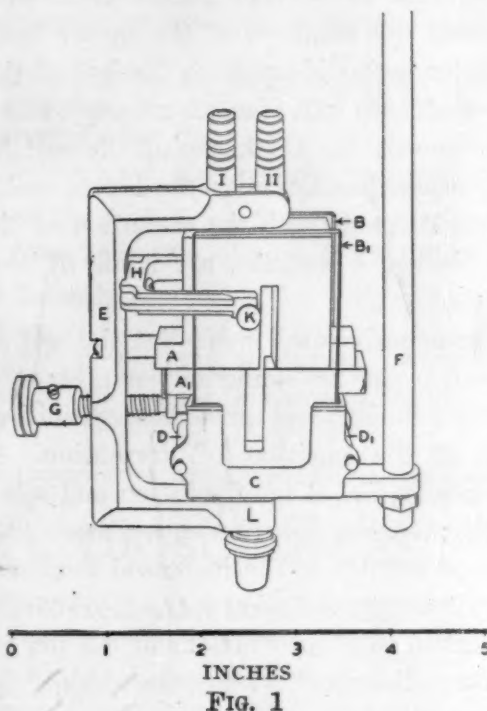
AN IMPROVED CELL FOR OPTICAL DIFFUSION MEASUREMENTS ON SOLUTIONS¹

MEASUREMENTS of the absolute diffusion rate in solutions require transparent cells in which the original boundary between solvent and solution and its spreading incidental to diffusion can be recorded photographically by either light absorption or light refraction methods.^{2,3}

The stainless steel cell of Lamm,⁴ now in general use, offers the great advantage of plane parallel glass windows that eliminate optical distortions seen with cylindrical glass tubes. On the other hand, boundary formation in the Lamm cell, accomplished by gradual withdrawal of a steel or bakelite diaphragm separating solvent from underlying solution, causes displacement of the upper column of liquid which may adversely influence the diffusion measurements when a high degree of precision is required.

To eliminate this difficulty, a simple diffusion cell of small volume has been designed on the principle of the new Tiselius electrophoresis cell.⁵ In the cell described here, solvent and solution surfaces are in direct contact as the boundary is formed. However, unlike the conditions with the Tiselius cell, the boundary is formed in the photographic field and thus does not have to be moved by special compensating arrangements. This cell, somewhat similar to that of Loughborough and Stamm,⁶ has been designed and built in cooperation with Mr. H. S. Bush, instrument maker of Cornell University.

Two stainless steel blocks A and A₁, with rectangular slots, constructed as shown in Fig. 1, are placed



one above the other. The upper block is fixed at the top and the side to the frame, E. The lower block is pressed against the upper one by the spring at L and can be moved laterally by means of a screw, G. The sliding surfaces of the blocks and their vertical front and back surfaces are ground and polished flat to within 1/10,000 of an inch. Two optically flat glass windows, B and B₁, fit against the cell surfaces and, together with block A₁, are held in place by means of two brackets C and C₁ (the latter not shown), clamped together by the screws D and D₁. H is a C-shaped clamp attached loosely to E and carrying the screw K, which can be tightened to exert pressure on the upper part of the glass windows.⁷ The vertical

⁷ In a recent design of the cell, the attachment of the clamp H has been moved from the frame E to the rod F. This permits the screw K to be left tightened during boundary formation.

¹ This work has been made possible by a grant from the Rockefeller Foundation.

² A. Tiselius and D. Gross, *Kolloid. Z.*, 66: 12, 1934.

³ O. Lamm and A. Polson, *Biochem. J.*, 30: 528, 1936.

⁴ O. Lamm, *Nova acta regiae soc. scient. Upsaliensis* 10, No. 6, 1937.

⁵ A. Tiselius, *Trans. Farad. Soc.*, 33: 524, 1937.

⁶ D. L. Loughborough and A. J. Stamm, *J. Phys. Chem.*, 40: 1113, 1936.

rod F leads to an attachment by which the cell is mounted in the constant temperature bath. I and II are cylindrical openings through which the cell is filled. By sliding the lower block to the left until its slit is in line with tube I, the lower compartment is completely shut off from the upper one. This part of the cell can be filled with solution through tube I, which connects through a one-eighth inch hole drilled through the upper block. The upper compartment is filled with the solvent through tube II. After the cell has been placed in the constant temperature bath, the screw K is loosened slightly, and the lower block, together with the glass plates, is moved slowly to the right until the upper and lower compartments are in alignment. Then the screw K is tightened again and diffusion proceeds.

A very thin layer of stop-cock grease is applied to the steel surfaces before the glass windows are set in place. In order to prevent grease from soiling the glass forming the windows of the upper half of the cell, a quarter-inch wide area to the left of the upper rectangular slot is left free of grease. For greater refraction power, the thickness of the cell has been increased, in comparison with the Lamm cell, from 1 to 1.7 cm. All parts with the exception of the stainless steel blocks, A and A₁, are made of chromium-plated brass.

From an experimental viewpoint the cell has been found to offer the following advantages: 1. Smooth boundary formation and immediate visibility of the boundary at the position of formation. 2. Small volume capacity, i.e., 2 cc of solution and solvent each being sufficient for a diffusion experiment. 3. Greater refractive power due to the increased thickness of the cell; this allows the diffusion rate of protein solutions to be measured in concentrations of 0.2 per cent. and less. 4. Easy dismantling and reassembling for cleaning purposes.

The cell has proved to be suitable for diffusion measurements with solutions of proteins as well as of low molecular weight substances, the results of which will be published elsewhere.

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A SIMPLE, THIN AQUARIUM

A SATISFACTORY, water-tight, live chamber can be built easily with two sheets of clear window glass, a length of heavy-walled "pressure" rubber tubing, two wooden rectangles of the same size as the glass and four C-clamps. The figure shows the separate parts and the assembly in end view. This unit will hold water, can be made in any size or shape needed, and, for photographic work with artificial backgrounds placed behind the assembly, is excellent, since it does

not distort the backgrounds or cause lack of uniformity in illumination.

If a thicker cell is wanted and rubber tubing of the largest size not adequate, a still broader unit can be made by adding a flat wooden rectangle and another U of tubing to the sandwich. Thus the thick cell will consist of rectangle—glass—tubing—rectangle—tubing—glass—rectangle. Smaller tubing can then be used and the flat rectangle made any thickness needed.

With this type of thin aquarium, all sorts of interesting lighting can be employed and many scenic backgrounds provided. Yet the organisms can not get far enough away from the front glass to escape a hand lens or dissecting binocular used horizontally.

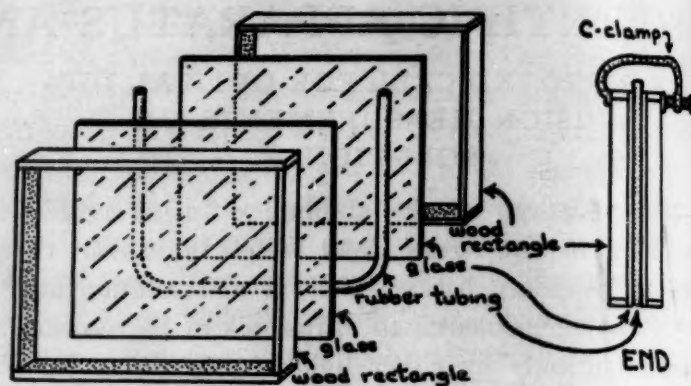


FIG. 1

For study of water insects, salamanders or fish, this type of equipment is much preferable to the commonly used thin museum jars, since it lacks distortion and can be made of any dimensions desired.

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BOOKS RECEIVED

- CHAMPION, F. C. *University Physics: Part I, General Physics*. Pp. 157. Illustrated. \$1.50. *Part II, Heat*. Pp. 148. Illustrated. \$1.50. Interscience.
- COLEMAN, A. P. *The Last Million Years. A History of the Pleistocene in North America*. Pp. xii + 216. Illustrated. University of Toronto Press. \$3.50.
- ELDER, ALBERT L. *Textbook of Chemistry*. Pp. viii + 751. Illustrated. Harper. \$3.75.
- HAMILTON, BURTON E. and K. JEFFERSON THOMSON. *The Heart in Pregnancy and the Childbearing Age*. Pp. viii + 402. Illustrated. Little, Brown. \$5.00.
- HOBBS, WILLIAM H., Editor. *Reports of the Greenland Expeditions of the University of Michigan. Part II, Meteorology, Physiography and Botany*. Pp. vii + 287. Illustrated. University of Michigan Press. \$5.00.
- HOSKINS, R. G. *Endocrinology; the Glands and their Functions*. Pp. 388. Illustrated. Norton. \$4.00.
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- PERLA, DAVID and JESSIE MARMORSTON. *Natural Resistance and Clinical Medicine*. Pp. xx + 1344. 15 figures. Little, Brown.
- ROBERTS, J. K. *Heat and Thermodynamics*. Third edition. Pp. xvi + 488. Illustrated. Interscience. \$5.50.
- TAYLOR, LLOYD W. *Physics, the Pioneer Science*. Pp. xii + 847 + xlv. Houghton Mifflin. \$4.00.